20 48
39 49
54,55

Welcome to DIALOG

Dialog level 02.08.05D

Last logoff: 05jul02 09:16:35
Logon file405 06aug02 08:34:29
? b 411
06aug02 08:34:40 User217743 Session D563.2
$0.00 0.073 DialUnits File410
$0.00 Estimated cost File410
$0.03 TELNET
$0.03 Estimated cost this search
$0.03 Estimated total session cost 0.234 DialUnits
File 411:DIALINDEX(R)

DIALINDEX(R)
(c) 2002 The Dialog Corporation plc

*** DIALINDEX search results display in an abbreviated *** *** format unless you enter the SET DETAIL ON command. *** ? set files allscience
You have 260 files in your file list.
(To see banners, use SHOW FILES command)
? s (ha or hyaluronic()acid or hyaluronan)()receptor

Your SELECT statement is:
s (ha or hyaluronic()acid or hyaluronan)()receptor

Items	File
2	2: INSPEC_1969-2002/Aug W1
310	5: Biosis Previews(R)_1969-2002/Jul W4
5	6: NTIS_1964-2002/Aug W2
2	8: Ei Compendex(R)_1970-2002/Aug W1
2	10: AGRICOLA_70-2002/Jul
1	16: Gale Group PROMT(R)_1990-2002/Aug 06
1	19: Chem.Industry Notes_1974-2002/ISS 200232
3	20: Dialog Global Reporter_1997-2002/Aug 06
1	28: Oceanic Abst._1964-2002/Jul
1030	34: SciSearch(R) Cited Ref Sci_1990-2002/Aug W1
19	35: Dissertation Abs Online_1861-2002/Jul
6	44: Aquatic Sci&Fish Abs_1978-2002/Jul
1	47: Gale Group Magazine DB(TM)_1959-2002/Aug 05
5	50: CAB Abstracts_1972-2002/Jul
14	65: Inside Conferences_1993-2002/Aug W1
141	71: ELSEVIER BIOBASE_1994-2002/Aug W1
224	73: EMBASE_1974-2002/Jul W4
1	74: Int.Pharm.Abs._1970-2002/Jul
81	76: Life Sciences Collection_1982-2002/Jul
12	77: Conference Papers Index_1973-2002/Jul
Examined 50 files	
1	91: MANTIS(TM)_1880-2002/Oct
10	94: JICST-EPlus_1985-2002/Jun W2
17	98: General Sci Abs/Full-Text_1984-2002/Jun
2	99: Wilson Appl. Sci & Tech Abs_1983-2002/Jun
1	103: Energy SciTec_1974-2002/Jul B1
1	107: Adis R&D Insight_1986-2002/Jul W4
1	128: PHARMAPROJECTS_1980-2002/Jul W4
23	143: Biol. & Agric. Index_1983-2002/Jun
84	144: Pascal_1973-2002/Aug W1
3	148: Gale Group Trade & Industry DB_1976-2002/Aug 06
4	149: TGG Health&Wellness DB(SM)_1976-2002/Jul W4
240	155: MEDLINE(R)_1966-2002/Jul W4
20	156: ToxFile_1965-2002/Jul W4
7	172: EMBASE Alert_2002/Aug W1
2	185: Zoological Record Online(R)_1978-2002/Jul
Examined 100 files	
4	266: FEDRIP_2002/Jun
2	285: BioBusiness(R)_1985-1998/Aug W1
2	286: Biocommerce Abs.& Dir._1981-2002/Jul B2
1	292: GEOBASE(TM)_1980-2002/Jul
2	315: ChemEng & Biotec Abs_1970-2002/Jun
Examined 150 files	
5	340: CLAIMS(R)/US Patent_1950-02/Aug 01
2	342: Derwent Patents Citation Indx_1978-01/200209C
5	345: Inpadoc/Fam.& Legal Stat_1968-2002/UD=200229
12	348: EUROPEAN PATENTS_1978-2002/Jul W04
70	349: PCT FULLTEXT_1983-2002/UB=20020801,UT=20020725
1	354: Ei EnCompassLit(TM)_1965-2002/Aug W1
5	357: Derwent Biotech Res._1982-2002/June W1
2	358: Current BioTech Abs_1983-2001/Oct
21	398: CHEMSEARCH(TM)_1957-2002/Jun
123	399: CA SEARCH(R)_1967-2002/UD=13706
349	440: Current Contents Search(R)_1990-2002/Aug 06
3	441: ESPICOM Pharm&Med DEVICE NEWS_2002/Jun W4
1	442: AMA Journals_1982-2002/Jun B3
2	444: New England Journal of Med._1985-2002/Aug W1
2	455: Drug News & Perspectives_1992-2002/Jul
1	459: Daily Essentials (Archival)_1996-2002/Jul W2
Examined 200 files	
11	484: Periodical Abs Plustext_1986-2002/Jul W4
1	613: PR Newswire_1999-2002/Aug 06
1	621: Gale Group New Prod.Annou.(R)_1985-2002/Aug 06
1	624: McGraw-Hill Publications_1985-2002/Aug 05
3	636: Gale Group Newsletter DB(TM)_1987-2002/Aug 06
2	649: Gale Group Newswire ASAP(TM)_2002/Aug 02
23	654: US PAT.FULL._1976-2002/Jul 30
Examined 250 files	
1	765: Frost & Sullivan_1992-1999/Apr
1	810: Business Wire_1986-1999/Feb 28

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        1   813: PR Newswire_1987-1999/Apr 30

  66 files have one or more items; file list includes 260
files.
? rf
Your last SELECT statement was:
  S (HA OR HYALURONIC()ACID OR
HYALURONAN)()RECEPTOR

Ref      Items  File
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N1        1030   34: SciSearch(R) Cited Ref
Sci_1990-2002/Aug W1 N2          349   440: Current
Contents Search(R)_1990-2002/Aug 06 N3          310
5: Biosis Previews(R)_1969-2002/Jul W4 N4          240
155: MEDLINE(R)_1966-2002/Jul W4
N5         224   73: EMBASE_1974-2002/Jul W4
N6         141   71: ELSEVIER BIOBASE_1994-2002/Aug
W1
N7         123   399: CA
SEARCH(R)_1967-2002/UD=13706
N8          84   144: Pascal_1973-2002/Aug W1
N9          81   76: Life Sciences
Collection_1982-2002/Jul N10          70   349: PCT
FULLTEXT_1983-2002/UB=20020801,UT=20020725
66 files have one or more items; file list includes 260
files.
      - Enter P or PAGE for more -
? b n4, n1
     06aug02 08:38:17 User217743 Session D563.3
        $10.47    5.982 DialUnits File411
   $10.47  Estimated cost File411
    $0.86  TELNET
   $11.33  Estimated cost this search
   $11.36  Estimated total session cost   6.217 DialUnits
SYSTEM:OS  - DIALOG OneSearch
  File 155:MEDLINE(R)  1966-2002/Jul W4
*File 155: Alert feature enhanced for multiple files,
duplicates removal, customized scheduling. See HELP
ALERT.
  File  34:SciSearch(R) Cited Ref Sci  1990-2002/Aug W1
       (c) 2002 Inst for Sci Info
*File  34: Alert feature enhanced for multiple files,
duplicates removal, customized scheduling. See HELP
ALERT.

    Set  Items  Description
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? s (ha or hyaluronic()acid or hyaluronan)()receptor
        55698  HA
        12932  HYALURONIC
      1893852  ACID
        12909  HYALURONIC(W)ACID
         5761  HYALURONAN
       942793  RECEPTOR
    S1    1270  (HA OR HYALURONIC()ACID OR
HYALURONAN)()RECEPTOR ? s s1 and py>2000
        1270  S1
     2283244  PY>2000
    S2     103  S1 AND PY>2000
? s s1 not s2
        1270  S1
         103  S2
    S3    1167  S1 NOT S2
? s s3 and hare
        1167  S3
        3342  HARE
    S4       5  S3 AND HARE
? s s3 and (175 or 190 or 300 or 315)()kd
        1167  S3
       23010  175
       24669  190
      177407  300
        8775  315
       62068  KD
         512  (((175 OR 190) OR 300) OR 315)(W)KD
    S5       0  S3 AND (175 OR 190 OR 300 OR 315)()KD
? s s3 and (ha or hyaluronan or hyaluronic or
chondroitin)/ti          1167  S3
        3705  HA/TI
        2783  HYALURONAN/TI
        2679  HYALURONIC/TI
        2973  CHONDROITIN/TI
    S6     295  S3 AND (HA OR HYALURONAN OR
HYALURONIC OR CHONDROITIN)/TI ? rd
...examined 50 records  (50)
...examined 50 records  (100)
...examined 50 records  (150)
...examined 50 records  (200)
...examined 50 records  (250)
...completed examining records
    S7     191  RD (unique items)
? t s7/3,ab/all

 7/3,AB/1     (Item 1 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

10985115  20545519  PMID: 10952975
  Identification of the *hyaluronan* *receptor* for
endocytosis (HARE).
  Zhou B; Weigel J A; Fauss L; Weigel P H
  Department of Biochemistry & Molecular Biology,
University of Oklahoma Health Sciences Center,
Oklahoma City, Oklahoma 73190, USA.  Journal of
biological chemistry (UNITED STATES)  Dec 1 2000,
275 (48) p37733-41, ISSN 0021-9258  Journal Code:
2985121R
  Contract/Grant No.: GM35978; GM; NIGMS
  Document type: Journal Article
  Languages: ENGLISH
  Main Citation Owner: NLM
  Record type: Completed
```

Rat liver sinusoidal endothelial cells (LECs) express two hyaluronan (HA) receptors, of 175 and 300 kDa, responsible for the endocytic clearance of HA. We have characterized eight monoclonal antibodies (mAbs) raised against the 175-kDa *HA* *receptor* partially purified from rat LECs. These mAbs also cross-react with the 300-kDa *HA* *receptor*. The 175-kDa *HA* *receptor* is a single protein, whereas the 300-kDa species contains three subunits, alpha, beta, and gamma at 260, 230, and 97 kDa, respectively (Zhou, B., Oka, J. A., and Weigel, P. H. (1999) J. Biol. Chem. 274, 33831-33834). The 97-kDa subunit was not recognized by any of the mAbs in Western blots. Based on their cross-reactivity with these mAbs, the 175-, 230-, and 260-kDa proteins appear to be related. Two of the mAbs inhibit (125)I-HA binding and endocytosis by LECs at 37 degrees C. All of these results confirm that the mAbs recognize the bone fide LEC *HA* *receptor*. Indirect immunofluoresence shows high protein expression in liver sinusoids, the venous sinuses of the red pulp in spleen, and the medullary sinuses of lymph nodes. Because the tissue distribution for this endocytic *HA* *receptor* is not unique to liver, we propose the name HARE (*HA* *receptor* for endocytosis).

7/3,AB/2 (Item 2 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

10898576 20457547 PMID: 11002457

The cytosolic *hyaluronic* acid level defines several clinico-biological properties of CD44v5-positive infiltrating ductal carcinoma of the breast]

La concentracion de acido hialuronico citosolico define ciertas propiedades clinicobiologicas del carcinoma ductal infiltrante de mama CD44v5 positivo.

Ruibal A; Arias J I; Carmen del Rio M; San Roman J M; Lapena G; Schneider J; Tejerina A

Servicio de Medicina Nuclear, Fundacion Jimenez Diaz, Madrid. Medicina clinica (SPAIN) Jul 8 2000, 115 (6) p201-7, ISSN 0025-7753 Journal Code: 0376377

Document type: Journal Article ; English Abstract

Languages: SPANISH

Main Citation Owner: NLM

Record type: Completed

BACKGROUND: The hyaluronic acid (HA) is a ligand of CD44 adhesion molecule. In this work, we study if the cytosolic level of this proteoglycan can modulate certain clinical-biological properties at CD44v5-positive infiltrating ductal carcinomas (IDC) of the breast. PATIENTS AND METHODS: We have assayed, by a radioligand method, the cytosolic level of hyaluronic acid in 127 IDC. Likewise, cytosolic levels of estrogen receptors (ER), progesterone receptors (PR), pS2, cathepsin D and tissue.-type plasminogen activators (t-PA) have been dossified, as well as those of epidermal growth factor receptor (EGFR) at cell surfaces. The menopausal status, tumor size, axillary lymph node involvement, histological grade, ploidy and S-phase have also been taken into account. RESULTS: HA positive (> 4800 ng/mg prt., which represents the median value obtained with 252 tumors) carcinomas had higher levels of PR (p = 0.035) and t-PA (p = 0.000), whereas HA negative showed a higher frequency of a tumor size > 2 cm (p = 0.015), aneuploidy (p = 0.015) and S-phase > 14% (p = 0.019), as well as histological grade 3 which reached statistical significance (p = 0.062), all of which were indicators of a worse behaviour and evolution. CONCLUSIONS: Our results suggest that, as it also happens with that of the cell surface, cytosolic HA levels seems to modulate certain clinical-biological features of CD44v5-positive infiltrating ductal carcinomas of the breast. Likewise, they can help us to explain the discordant results described at the literature concerning its practical value when each of them are considered separately.

7/3,AB/3 (Item 3 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

10871740 20428667 PMID: 10882722

Differences in *hyaluronic* acid-mediated functions and signaling in arterial, microvessel, and vein-derived human endothelial cells.

Lokeshwar V B; Selzer M G

Departments of Urology and Cell Biology and Anatomy, University of Miami School of Medicine, Miami, Florida 33101, USA. vlokeshw@med.miami.edu Journal of biological chemistry (UNITED STATES) Sep 8 2000, 275 (36) p27641-9, ISSN 0021-9258 Journal Code: 2985121R

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: Completed

Hyaluronic acid (HA), a nonsulfated glycosaminoglycan, regulates cell adhesion and migration. Small HA fragments (3-25 disaccharide units) induce neovascularization. We investigated the effect of HA and a HA fragment (10-15 disaccharide units, F1) on primary human endothelial cells (ECs). Human pulmonary ECs (HPAEC) and lung microvessel ECs (HMVEC-L) bound HA (K(d) approximately 1 and 2.3 nm, respectively) and expressed 17,780 and 16,690 HA binding sites, respectively. Both ECs showed HA-mediated cell adhesion; however, HMVEC-L was 1.5-fold better. Human umbilical vein ECs neither bound HA nor showed HA-mediated adhesion. All three ECs expressed CD44 (approximately 110 kDa). The expression of receptor for HA-mediated motility (RHAMM) (approximately 80 kDa) was the highest in HMVEC-L, followed by HPAEC and human umbilical vein ECs. RHAMM, not CD44, bound HA in all

three ECs. F1 was better than HA and stimulated a 2. 5- and 1.8-fold mitogenic response in HMVEC-L and HPAEC, respectively. Both HA and F1 induced tyrosine phosphorylation of p125(FAK), paxillin, and p42/44 ERK in HMVEC-L and HPAEC, which was blocked by an anti-RHAMM antibody. These results demonstrate that RHAMM is the functional *HA* *receptor* in primary human ECs. Heterogeneity exists among primary human ECs of different vascular origins, with respect to functional *HA* *receptor* expression and function.

7/3,AB/4 (Item 4 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

10754795 20309751 PMID: 10751416
Oncostatin M and transforming growth factor-beta 1 induce post-translational modification and *hyaluronan* binding to CD44 in lung-derived epithelial tumor cells.
Cichy J; Pure E
Wistar Institute, Philadelphia, Pennsylvania 19104, USA.
Journal of biological chemistry (UNITED STATES) Jun 16 2000, 275 (24) p18061-9, ISSN 0021-9258 Journal Code: 2985121R
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
CD44, a receptor for hyaluronan (HA), has been implicated in tumor growth and metastasis. Most CD44-positive cells fail to exhibit constitutive *HA* *receptor* function but CD44-mediated HA binding on hematopoetic cells can be induced by antibody cross-linking of the receptor and by physiologic stimuli, including cytokines. We now demonstrate that oncostatin M (OSM) and transforming growth factor-beta1, cytokines known to regulate the growth of tumor cells, stimulate HA binding in lung epithelial-derived tumor cells. In lung epithelial-derived tumor cells, cytokine-induced binding resulted from post-translational modification of the receptor. OSM-induced HA binding was associated with a reduction in N-linked carbohydrate content of CD44. In addition, OSM induced HA binding via a novel mechanism requiring sulfation of chondroitin sulfate chains linked to CD44. The mechanism underlying transforming growth factor-beta1 induced HA binding was distinct from the effects of OSM. The data presented indicate that modulation of the glycosylation and sulfation of CD44 by cytokines provides mechanisms for regulating cell adhesion during tumor growth and metastasis.

7/3,AB/5 (Item 5 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

10730511 20267381 PMID: 10809384
Are *hyaluronan* receptors involved in three-dimensional cell migration?
Nehls V; Hayen W
Department of Medicine, Institute for Clinical Biochemistry and Pathobiochemistry, University of Wurzburg, Germany. nehls@klinbiochem.uni-w uerzburg.de
Histology and histopathology (SPAIN) Apr 2000, 15 (2) p629-36, ISSN 0213-3911 Journal Code: 8609357
Document type: Journal Article; Review; Review, Tutorial
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
Hyaluronan (HA), an unbranched polysaccharide consisting of repeated glucuronic acid/N-acetylglucosamine disaccharide units, is ubiquitously present in the extracellular matrix of many tissues (for a more comprehensive review see: Fraser et al., 1997). Increased amounts of hyaluronan are produced by solid tumors and tumor-associated fibroblasts, and tumor-induced HA is correlated with poor prognosis. HA is well known to stimulate the migration of a large variety of cell types. Stimulation of cell migration by HA has been explained by different mechanisms. HA was shown to specifically bind to cell surface receptors, and inhibition of *HA*-*receptor* function was demonstrated to decrease cell migration and tumor growth. On the other hand, HA as a large hydrophilic molecule is also known to modulate the extracellular packing of collagen and fibrin, leading to increased fiber size and porosity of extracellular substrates. Hence a modified matrix architecture might similarly account for increased locomotion of cells. In this review, we attempted to summarize the available data on HA-induced cell migration, with particular emphasis on the role of HA receptors in three-dimensional cell migration. Although the *HA* *receptor* CD44 has been shown to mediate migration of cells over two-dimensional hyaluronan-coated surfaces in vitro, there is only little evidence that HA-binding to CD44 or other HA receptors has major impact on the locomotion of cells through three-dimensional matrices in vivo. We showed recently that the promigratory effect of HA in fibrin gels is largely due to HA-mediated modulation of fibrin polymerization. By increasing the porosity of fibrin gels, HA strongly accelerates cell migration. The porosity of matrices therefore appears as an important and probably underestimated determinant of cell migration and tumor spread.

7/3,AB/6 (Item 6 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

10660836 20192996 PMID: 10730753
Topical hyaluronidase decreases *hyaluronic* acid and CD44 in human skin and in reconstituted human epidermis: evidence that hyaluronidase can permeate the stratum corneum.
Laugier J P; Shuster S; Rosdy M; Csoka A B; Stern R; Maibach H I Department of Dermatology, School of Medicine, University of California San Francisco, 94143-0506, USA.
British journal of dermatology (ENGLAND) Feb 2000, 142 (2) p226-33, ISSN 0007-0963 Journal Code: 0004041
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
Hyaluronic acid (HA), a high molecular weight glycosaminoglycan of the extracellular matrix involved in growth, inflammation and wound healing, also contributes to the hydration and plastic properties of skin. Several drug and cosmetic formulations contain HA. We have initiated investigations that explore whether it is possible, by topical application, to modulate endogenous HA levels in skin. We developed a model epidermal culture system that exhibited a differentiated stratum corneum, and expressed HA and the *HA* *receptor* CD44, in a pattern similar to that observed in intact skin. Such in vitro skin equivalents are useful models for investigating the effect of topical drugs. HA and bacterial hyaluronidase were applied to the in vitro skin equivalent and to human skin. Their effects on endogenous HA and CD44 expression were examined using histochemical analysis. Topical HA treatment had no significant effect on HA or CD44 expression in either system. However, hyaluronidase decreased HA and CD44 expression in a dose-dependent manner in both the epidermal culture system and in skin. Apparently, HA is not able to permeate the epidermal culture system or human skin to a significant degree, but bacterial hyaluronidase does permeate both human skin and the culture system, depleting HA and decreasing CD44 expression. These effects were more prominent in the dermal than in the epidermal layers, suggesting that marked differences in HA metabolism exist in these two skin compartments. The ability of hyaluronidase to permeate the stratum corneum suggests that topical application may, additionally, be useful as a clinical modality.

7/3,AB/7 (Item 7 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

10638645 20179901 PMID: 10713114
Heparan sulfate proteoglycan isoforms of the CD44 *hyaluronan* *receptor* induced in human inflammatory macrophages can function as paracrine regulators of fibroblast growth factor action.
Jones M; Tussey L; Athanasou N; Jackson D G Department of Cellular Science, John Radcliffe Hospital, Headington, Oxford OX3 9DU, United Kingdom.
Journal of biological chemistry (UNITED STATES) Mar 17 2000, 275 (11) p7964-74, ISSN 0021-9258 Journal Code: 2985121R
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
The CD44 glycoprotein is expressed in multiple isoforms on a variety of cell types where it functions as a receptor for hyaluronan-mediated motility. Recently, interest has centered on CD44 heparan sulfate proteoglycan (HSPG) isoforms because of their potential to sequester heparin-binding growth factors and chemokines. Expression of these isoforms on ectodermal cells has recently been shown to regulate limb morphogenesis via presentation of fibroblast growth factor (FGF) 4/FGF 8 while expression on tumor cells was shown to sequester hepatocyte growth factor and promote tumor dissemination. To date, however, CD44 HSPG expression in tissue macrophages and lymphocytes has not been adequately investigated, despite the fact these cells actively synthesize growth factors and chemokines and indirect evidence that monocyte CD44 sequesters macrophage inflammatory protein-1beta. Here we show primary human monocytes rather than lymphocytes express CD44 HSPGs, but only following in vitro differentiation to macrophages or activation with the proinflammatory cytokine interleukin-1alpha or bacterial lipopolysaccharide. Furthermore, we show these isoforms are preferentially modified with heparan rather than chondroitin sulfate, bind the macrophage-derived growth factors FGF-2, vascular endothelial growth factor, and heparin-binding epidermal growth factor with varying affinities (K(d) 25-330 nM) and in the case of FGF-2, can stimulate productive binding to the high affinity tyrosine kinase FGF receptor 1 (FGFR1). In contrast, we find no evidence for significant binding to C-C chemokines. Last, we confirm by immunofluorescent antibody staining that inflamed synovial membrane macrophages express CD44 HSPGs and that expression is greatest in cells containing high FGF-2 levels. These results suggest a paracrine role for macrophage CD44 HSPG isoforms in the regulation of growth factor action during inflammation.

7/3,AB/8 (Item 8 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

10515392 20036507 PMID: 10567337
Purification and subunit characterization of the rat

liver endocytic *hyaluronan* *receptor*.
Zhou B; Oka J A; Singh A; Weigel P H
Department of Biochemistry, University of Oklahoma Health Sciences Center, Oklahoma City, Oklahoma 73190, USA.
Journal of biological chemistry (UNITED STATES) Nov 26 1999, 274 (48) p33831-4, ISSN 0021-9258 Journal Code: 2985121R
Contract/Grant No.: GM35978; GM; NIGMS
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
The endocytic hyaluronan (*HA*) *receptor* of liver sinusoidal endothelial cells (LECs) is responsible for the clearance of HA and other glycosaminoglycans from the circulation in mammals. We report here for the first time the purification of this liver *HA* *receptor*. Using lectin and immuno-affinity chromatography, two *HA* *receptor* species were purified from detergent-solubilized membranes prepared from purified rat LECs. In nonreducing SDS-polyacrylamide gel electrophoresis (PAGE), these two proteins migrated at 175- and approximately 300 kDa corresponding to the two species previously identified by photoaffinity labeling of live cells as the *HA* *receptor* (Yannariello-Brown, J., Frost, S. J., and Weigel, P. H. (1992) J. Biol. Chem. 267, 20451-20456). These two proteins co-purify in a molar ratio of 2:1 (175:300), and both proteins are active, able to bind HA after SDS-PAGE, electrotransfer, and renaturation. After reduction, the 175-kDa protein migrates as a approximately 185-kDa protein and is not able to bind HA. The 300-kDa *HA* *receptor* is a complex of three disulfide-bonded subunits that migrate in reducing SDS-PAGE at approximately 260, 230, and 97 kDa. These proteins designated, respectively, the alpha, beta, and gamma subunits are present in a molar ratio of 1:1:1 and are also unable to bind HA when reduced. The 175-kDa protein and all three subunits of the 300-kDa species contain N-linked oligosaccharides, as indicated by increased migration in SDS-PAGE after treatment with N-glycosidase F. Both of the deglycosylated, nonreduced *HA* *receptor* proteins still bind HA.

7/3,AB/9 (Item 9 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

10498162 20016350 PMID: 10547355
The intracellular *hyaluronan* *receptor* RHAMM/IHABP interacts with microtubules and actin filaments.
Assmann V; Jenkinson D; Marshall J F; Hart I R
Richard Dimbleby Department of Cancer Research/ICRF Laboratory, St Thomas' Hospital, Lambeth Palace Road, London SE1 7EH, UK. V.Assmann@icrf.icnet.uk
Journal of cell science (ENGLAND) Nov 1999, 112 (Pt 22) p3943-54, ISSN 0021-9533 Journal Code: 0052457
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
We reported recently on the intracellular localisation of the *hyaluronan* *receptor* RHAMM/IHABP in human cancer cells. Here we describe the colocalisation of RHAMM/IHABP proteins with microtubules, both in interphase and dividing cells, suggesting that RHAMM/IHABP represents a novel member of the family of microtubule-associated proteins (MAPs). We have identified four different splice variants of RHAMM/IHABP, all of which colocalise, at least transiently, with microtubules when expressed as GFP fusion proteins in HeLa cells. Using microtubule-binding assays and transient transfection experiments of deletion-bearing RHAMM/IHABP mutants, we localised the microtubule-binding region to the extreme N terminus of RHAMM/IHABP. This interaction domain is composed of two distinct subdomains, one of which is sufficient to mediate binding to the mitotic spindle while both domains are required for binding of RHAMM/IHABP proteins to interphase microtubules. Sequence analysis revealed that the projection domain of RHAMM/IHABP is predicted to form coiled-coils, implying that RHAMM/IHABP represents a filamentous protein capable of interacting with other proteins and we found that RHAMM/IHABP interacts with actin filaments in vivo and in vitro. Moreover, in vitro translated RHAMM/IHABP isoforms efficiently bind to immobilised calmodulin in a Ca(2+)-dependent manner via a calmodulin-binding site within the projection domain of RHAMM/IHABP (residues 574-602). Taken together, our results strongly suggest that RHAMM/IHABP is a ubiquitously expressed, filamentous protein capable of interacting with microtubules and microfilaments and not, as numerous previous reports suggest, a cell surface receptor for the extracellular matrix component hyaluronan.

7/3,AB/10 (Item 10 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

10493214 20019657 PMID: 10550319
Identification and characterization of three cDNAs that encode putative novel *hyaluronan* -binding proteins, including an endothelial cell-specific *hyaluronan* *receptor*.
Tsifrina E; Ananyeva N M; Hastings G; Liau G
Department of Vascular Biology, Jerome H. Holland

Laboratory, American Red Cross, Rockville, Maryland, USA.
American journal of pathology (UNITED STATES) Nov 1999, 155 (5) p1625-33, ISSN 0002-9440 Journal Code: 0370502
Contract/Grant No.: HL37510; HL; NHLBI
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
The glycosaminoglycan hyaluronan (HA) and HA-binding proteins (HABPs) serve important structural and regulatory functions during development and in maintaining adult tissue homeostasis. Here we have identified and partially characterized the sequence and expression pattern of three putative novel HABPs. DNA sequence analysis revealed that two of the novel HABPs, WF-HABP and BM-HABP, form a unique HA-binding subfamily, whereas the third protein, OE-HABP, is more closely related to the LINK subfamily of HABPs. Northern blotting experiments revealed that the expression of BM-HABP was highly restricted, with substantial expression detected only in human fetal liver. In contrast, WF-HABP and OE-HABP mRNAs were detected in a number of tissues, with particularly prominent expression in highly vascularized tissues such as the heart, placenta, and lung. Additional studies showed that OE-HABP was expressed by cultured human endothelial cells, smooth muscle cells, and differentiated monocytes. However, only endothelial cells expressed WF-HABP mRNA, and its expression was regulated by growth state, being most prominent in quiescent endothelial cells. We further characterized the expression of WF-HABP in vivo and found that its expression colocalized with CD31-positive cells and was prominently expressed in microvessels in the human aorta and in atherectomy samples. Our data suggest that WF-HABP is an endothelial cell-specific *HA* *receptor* and that it may serve a unique function in these cells. The WF-HABP gene was localized to chromosome 3p21.31 and the OE-HABP gene to 15q25.2-25.3.

7/3,AB/11 (Item 11 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

10475709 20004618 PMID: 10534350
Characterization of a *hyaluronan* *receptor* on rat sinusoidal liver endothelial cells and its functional relationship to scavenger receptors.
McCourt P A; Smedsrod B H; Melkko J; Johansson S
Department of Experimental Pathology, University of Tromso, Tromso, Norway. petermcc@fagmed.uit.no
Hepatology (Baltimore, Md.) (UNITED STATES) Nov 1999, 30 (5) p1276-86, ISSN 0270-9139 Journal Code: 8302946
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
Hyaluronan is a widely distributed extracellular component of connective tissue with several mechanical and cell biological functions. The serum level of hyaluronan is elevated in rheumatic and liver diseases and in certain malignancies. The major route of hyaluronan clearance from the blood is via the liver, taken up predominantly by sinusoidal liver endothelial cells. We have purified a novel hyaluronan binding protein from liver that also has an affinity for the N-terminal propeptide of type I procollagen, a physiological scavenger receptor ligand. A polyclonal antibody raised against the protein was found to inhibit the binding and degradation of hyaluronan as well as two scavenger receptor ligands by cultured sinusoidal liver endothelial cells. Immunostaining of nonpermeabilized liver cells and liver sections showed that the antibody specifically stains the surface of sinusoidal liver endothelial cells. After pretreatment with monensin to block the recirculation of endocytic receptors, the immunostaining was specifically associated with early endosomes of these cells. Thus, this rat sinusoidal liver endothelial cell *hyaluronan* *receptor* shares functional properties with the scavenger receptor family, a group of proteins shown to play a key role in the uptake of atherogenic lipids and other waste products from the tissues.

7/3,AB/12 (Item 12 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

10463826 99458853 PMID: 10527620
Internalization of the *hyaluronan* *receptor* CD44 by chondrocytes.
Aguiar D J; Knudson W; Knudson C B
Rush Medical College, Rush-Presbyterian-St. Luke's Medical Center, 1653 W. Congress Parkway, Chicago, Illinois, 60612-3864, USA.
Experimental cell research (UNITED STATES) Nov 1 1999, 252 (2) p292-302, ISSN 0014-4827 Journal Code: 0373226
Contract/Grant No.: AR39239; AR; NIAMS; AR39507; AR; NIAMS; AR43384; AR; NIAMS
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
Chondrocytes express CD44 as a primary receptor for the matrix macromolecule hyaluronan. Hyaluronan is responsible for the retention and organization of proteoglycan within cartilage, and hyaluronan-chondrocyte interactions are important for the assembly and

maintenance of the cartilage matrix. Bovine articular chondrocytes were used to study the endocytosis and turnover of CD44 and the effects of receptor occupancy on this turnover. Matrix-intact chondrocytes exhibit approximately a 6% internalization of cell surface CD44 by 4 h. Treatment with Streptomyces hyaluronidase to remove endogenous pericellular matrix increased internalization to approximately 20% of cell surface CD44 at 4 h. This turnover could be partially inhibited by the addition of exogenous hyaluronan to these matrix-depleted chondrocytes. Cell surface biotin-labeled CD44 was internalized by chondrocytes and this internalization was decreased in the presence of hyaluronan. Colocalization of internalized CD44 and fluorescein-labeled hyaluronan in intracellular vesicles correlates with the previous results of receptor-mediated endocytosis pathway for the degradation of hyaluronan by acid hydrolases. Taken together, our results indicate that CD44 is internalized by chondrocytes and that CD44 turnover is modulated by occupancy with hyaluronan. Copyright 1999 Academic Press.

7/3,AB/13 (Item 13 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

10448956 99425070 PMID: 10493913
Synthesis and shedding of *hyaluronan* from plasma membranes of human fibroblasts and metastatic and non-metastatic melanoma cells. Luke H J; Prehm P
Institut fur Physiologische Chemie und Pathobiochemie, Waldeyerstr. 15, D-48129 Munster, Germany.
Biochemical journal (ENGLAND) Oct 1 1999, 343 Pt 1 p71-5, ISSN 0264-6021 Journal Code: 2984726R
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
The regulation of hyaluronan synthesis and shedding was analysed in human fibroblasts and in two melanoma cells that differed in the metastatic potential and proteolysis of the *hyaluronan* *receptor* CD44. Dissociation of nascent hyaluronan from plasma membranes isolated from fibroblasts by high salt concentrations led to activation of hyaluronan synthase. Hyaluronan synthesis was also enhanced in plasma membranes from fibroblasts that had been treated with hyaluronidase or trypsin. Hyaluronan oligosaccharides stimulated hyaluronan production in fibroblast cultures. These results indicated that nascent high-molecular-mass hyaluronan inhibited its own chain elongation, if it was retained in the vicinity of the synthase by cell-surface receptors. The results also indicated that increased hyaluronan synthesis and shedding correlated with proteolysis of CD44 on the melanoma cell lines, which has been observed by others.

7/3,AB/14 (Item 14 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

10398479 99385573 PMID: 10458391
The *hyaluronic* *acid* *receptor* is induced by stretch injury of rat bladder in vivo and influences smooth muscle cell contraction in vitro.
Bagli D J; Joyner B D; Mahoney S R; McCulloch L
Department of Surgery, Hospital For Sick Children, Research Institute, University of Toronto, Ontario, Canada.
Journal of urology (UNITED STATES) Sep 1999, 162 (3 Pt 1) p832-40, ISSN 0022-5347 Journal Code: 0376374
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
PURPOSE: Loss of bladder compliance from hypercontractility and fibrosis may represent an injury response to excessive intravesical pressure. Together, interactions between cell and extracellular matrix components regulate cell response to injury and extracellular matrix remodeling. The receptor for hyaluronic acid mediated motility (RHAMM) is a recently described hyaluronic acid binding protein known to influence multiple types of cell extracellular matrix interaction in development, injury and cancer. We evaluate the role of RHAMM in mediating early events in bladder stretch injury. MATERIALS AND METHODS: An acute stretch injury model was used. The rat bladder was injured by hydrodistention inducing gross hematuria. Tissues were analyzed for temporal and spatial expression of RHAMM in the mucosa and detrusor regions by immunostaining, western and reverse transcriptase polymerase chain reaction analyses. The contractile activity of smooth muscle cell primary cultures was analyzed using a gel contraction assay in the presence of peptide fragments known to block RHAMM function. RESULTS: Acute hydrodistention caused immediate and significant injury to the bladder, with fracturing of smooth muscle cell bundles, edema and hemorrhage. RHAMM immunolocalized to the mucosa and detrusor within 2 hours of injury, peaking by 5 to 10 hours. A shift from low molecular weight (55 kD.) to high (120 kD.) receptor isoforms was prominent during the peak expression period noted by immunolocalization. RHAMM messenger ribonucleic acid increased only slightly (40%) by 5 hours after injury. Smooth muscle cell primary cultures actively initiated and maintained the contraction of collagen gels by more than 75% of baseline in vitro. Blocking RHAMM function significantly inhibited the ability to less than 25% of smooth muscle cells to contract the gels in

vitro. CONCLUSIONS: Increased expression of RHAMM is an early event precipitated by stretch injury to the bladder. Since extracellular matrix hyaluronic acid is found early in tissue repair responses, its receptor RHAMM may be mediating initial bladder responses to stretch injury, some of which (contraction) may be experimentally blocked in vitro. Since the receptor directly regulates protein kinase signaling which in turn mediates smooth muscle cell contraction and collagen synthesis, further studies of RHAMM function in bladder pathology are warranted.

7/3,AB/15 (Item 15 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

10326002 99292812 PMID: 10362554
Hyaluronan stimulates tumor cell migration by modulating the fibrin fiber architecture.
Hayen W; Goebeler M; Kumar S; Riessen R; Nehls V
Medizinische Klinik; Institut fur Klinische Biochemie und Pathobiochemie der Universitat Wurzburg and Klinik und Poliklinik fur Haut- und Geschlechtskrankheiten, Josef-Schneider-Str. 2, Germany.
Journal of cell science (ENGLAND) Jul 1999, 112 (Pt 13) p2241-51, ISSN 0021-9533 Journal Code: 0052457
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
The glycosaminoglycan hyaluronan, which supports tumor cell migration and metastasis, interferes with fibrin polymerization and leads to increased fiber size and porosity of fibrin clots. Here we have studied the proportionate effect of fibrin polymerization on hyaluronan-mediated migration of glioblastoma cells. The structural and physical properties of hyaluronan-containing fibrin gels were analyzed by turbidity measurement, laser scanning microscopy, compaction assay, and calculation of pore size by liquid permeation. When fibrin polymerized in the presence of hyaluronan or dextran, the resulting gels strongly stimulated cell migration, and migration significantly correlated with fiber mass-to-length ratios and pore diameters. In contrast, cell migration was not induced by addition of hyaluronan to supernatants of already polymerized gels. Hyaluronan-mediated migration was inhibited in fibrin gels by antibodies to alphav- and beta1integrins and the disintegrin echistatin, but not by antibodies to the *hyaluronan* *receptor* CD44 (up to 50 microg/ml). As a control, we show that anti-CD44 (10 microg/ml) inhibited cell migration on a pure hyaluronan matrix using a two-dimensional Boyden chamber system. In contrast to three-dimensional migration, the migration of cells on the surfaces of variably structured fibrin gels was not significantly different, indicating that increased gel permeability (porosity) may account for hyaluronan-mediated migration. We conclude that, in complex three-dimensional substrates, the predominant effect of hyaluronan on cell migration might be indirect and requires modulation of fibrin polymerization.

7/3,AB/16 (Item 16 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

10309351 99317038 PMID: 10390150
CD44 expression and *hyaluronic* acid binding of malignant glioma cells.
Knupfer M M; Poppenborg H; Hotfilder M; Kuhnel K; Wolff J E; Domula M University Leipzig, Children's Hospital, Department of Pediatric Hematology and Oncology, Germany. knuem@server3.medizin.uni-leipzig.de
Clinical & experimental metastasis (NETHERLANDS) Feb 1999, 17 (1) p71-6, ISSN 0262-0898 Journal Code: 8409970
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
The mechanisms leading to rapid invasive growth of malignant gliomas are poorly understood. Expression of the hyaluronic acid (*HA*) *receptor* CD44 and adhesion to HA are involved in invasive properties. Our previous studies have shown that malignant glioma cells are able to adhere to extracellular HA. Here we investigated expression of the *hyaluronic* *acid* *receptor* CD44 protein in five human (T98G, A172, U87MG, 86HG39, 85HG66) and two rat (C6, 9L) glioma cell lines. Influence of anti-CD44 antibody and hyaluronidase-preincubation on the HA-binding was determined using HA/BSA (bovine serum albumin)-coated culture plates. While all gliomas were highly positive for CD44 with no differences in the number of positive staining cells, median fluorescence intensity decreased as follows: C6>T98G>9L>85HG66> 86HG39>A172>U87MG. Using HA/BSA coated culture plates the relative levels of specific adhesion to HA were determined as T98G>A172>9L>86HG39>U87MG> 85HG66. C6 cells failed to bind HA specifically. Incubation with anti-human-CD44 MAb significantly decreased HA-adhesion of T98G, A172, 85HG66 and U87MG human glioma cells. However the binding capacity was completely blocked only in 85HG66 cells. The three other cell lines kept a specific HA-adhesion after saturation of the receptor. Hyaluronidase pretreatment markedly enhanced HA-adhesion of C6 and 9L rat glioma cells. These results suggest that (i) HA-adhesion of malignant glioma cells is mainly, but not only, mediated by CD44, (ii) expression of CD44 does not correspond with adhesion capacity and (iii) cell-bound

glycosaminoglycans may influence glioma cell adhesion to extracellular HA.

7/3,AB/17 (Item 17 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

10296026 99280207 PMID: 10353740
Expression of the *hyaluronan* *receptor*, CD44S, in epithelial ovarian cancer is an independent predictor of survival.
Kayastha S; Freedman A N; Piver M S; Mukkamalla J; Romero-Guittierez M; Werness B A
Division of Pathology, Roswell Park Cancer Institute, Buffalo, New York 14263, USA.
Clinical cancer research : an official journal of the American Association for Cancer Research (UNITED STATES) May 1999, 5 (5) p1073-6, ISSN 1078-0432 Journal Code: 9502500
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
Most ovarian carcinomas present at advanced stage, principally as the result of dissemination to peritoneal sites. Standard CD44 (CD44S) is the principal receptor for hyaluronic acid, and in vitro and animal studies have suggested that the attachment of ovarian carcinoma cells to the peritoneal mesothelium involves the interaction between CD44S on ovarian carcinoma cells and hyaluronic acid on mesothelial surfaces. We, therefore, analyzed a series of ovarian carcinomas for the expression of CD44S by immunohistochemistry to see whether expression of this receptor by tumor cells correlated with clinicopathological factors and measures of patient outcome. Fifty-six fixed, paraffin-embedded primary epithelial ovarian tumors were immunostained with antibody to CD44S. Membrane staining was considered positive, and results were correlated with stage, grade, age, histology, and survival. Twenty-two (39%) tumors were positive for CD44S. There was no correlation between CD44 expression and histological type, grade, age, or stage. However, CD44 expression was significantly associated with survival in both univariate (P = 0.003) and multivariate (P = 0.006) analyses. These results support a role for CD44S expression in the spread of ovarian epithelial cancer and suggest that expression of this molecule is a significant independent predictor of survival in women with this disease.

7/3,AB/18 (Item 18 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

10246206 99233653 PMID: 10216086
Potential role for *hyaluronan* and the *hyaluronan* *receptor* RHAMM in mobilization and trafficking of hematopoietic progenitor cells.
Pilarski L M; Pruski E; Wizniak J; Paine D; Seeberger K; Mant M J; Brown C B; Belch A R
Departments of Oncology and Medicine, University of Alberta, Cross Cancer Institute, Edmonton, Alberta, Canada. lpilarsk@gpu.srv.ualberta.ca Blood (UNITED STATES) May 1 1999, 93 (9) p2918-27, ISSN 0006-4971 Journal Code: 7603509
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
Although the mechanism(s) underlying mobilization of hematopoietic progenitor cells (HPCs) is unknown, detachment from the bone marrow (BM) microenvironment and motility are likely to play a role. This work analyzes the motile behavior of HPCs and the receptors involved. CD34(+)45(lo/med)Scatterlo/med HPCs from granulocyte colony-stimulating factor (G-CSF)-mobilized blood and mobilized BM were compared with steady-state BM for their ability to bind hyaluronan (HA), their expression of the HA receptors RHAMM and CD44, and their motogenic behavior. Although RHAMM and CD44 are expressed by mobilized blood HPCs, function blocking monoclonal antibodies (MoAbs) identified RHAMM as a major HA binding receptor, with a less consistent participation by CD44. Permeabilization of mobilized blood HPCs showed a pool of intracellular (ic) RHAMM and a smaller pool of icCD44. In contrast, steady-state BM HPCs have significantly larger pools of icRHAMM and icCD44. Also, in contrast to mobilized blood HPCs, for steady-state BM HPCs, MoAbs to RHAMM and CD44 act as agonists to upregulate HA binding. The comparison between mobilized and steady-state BM HPCs suggests that G-CSF mobilization is associated with depletion of intracellular stores of HA receptors and modulates *HA* *receptor* usage. To confirm that mobilization alters the *HA* *receptor* distribution and usage by HPCs, samples of BM were collected at the peak of G-CSF mobilization in parallel with mobilized blood samples. *HA* *receptor* distribution of mobilized BM HPCs was closely matched with mobilized blood HPCs and different from steady-state BM HPCs. Mobilized BM HPCs had lower pools of icHA receptors, similar to those of mobilized blood HPCs. Treatment of mobilized BM HPCs with anti-RHAMM MoAb decreased HA binding, in contrast to steady-state BM HPCs. Thus, G-CSF mobilization may stimulate an autocrine stimulatory loop for HPCs in which HA interacts with basal levels of RHAMM and/or CD44 to stimulate receptor recycling. Consistent with this, treatment of HPCs with azide, nystatin, or cytochalasin B increased HA binding, implicating an energy-dependent process involving lipid rafts and the cytoskeleton. Of the

sorted HPCs, 66% were adherent and 27% were motile on fibronectin plus HA. HPC adherence was inhibited by MoAbs to beta1 integrin and CD44, but not to RHAMM, whereas HPC motility was inhibited by MoAb to RHAMM and beta1 integrin, but not to CD44. This finding suggests that RHAMM and CD44 play reciprocal roles in adhesion and motility by HPCs. The G-CSF-associated alterations in RHAMM distribution and the RHAMM-dependent motility of HPCs suggest a potential role for HA and RHAMM in trafficking of HPCs and the possible use of HA as a mobilizing agent in vivo.

7/3,AB/19 (Item 19 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

10243679 99226861 PMID: 10211879
Modulation of *hyaluronan* *receptor* (CD44) function in vivo in a murine model of rheumatoid arthritis.
Mikecz K; Dennis K; Shi M; Kim J H
Rush-Presbyterian-St. Luke's Medical Center, Chicago, Illinois 60612, USA.
Arthritis and rheumatism (UNITED STATES) Apr 1999, 42 (4) p659-68, ISSN 0004-3591 Journal Code: 0370605
Contract/Grant No.: AR-44126; AR; NIAMS
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
OBJECTIVE: To determine how in vivo modulation of CD44 function by antibodies influences disease severity in a murine model of rheumatoid arthritis. METHODS: Mice with proteoglycan (PG)-induced arthritis were subjected to systemic treatment with 3 different monoclonal antibodies against CD44. Joint swelling and serum levels of hyaluronan (HA) and soluble CD44 (sCD44) were monitored. Inflammatory leukocyte infiltration in the joints, cell surface CD44 expression, and leukocyte adhesion to HA were compared. The effects of anti-CD44 treatment on the immune status of arthritic animals were also determined. RESULTS: Antibody IRAWB14, which enhances HA binding, aggravated the inflammatory symptoms, while KM201, which blocks ligand binding, reduced the severity of arthritis. The most effective suppression of inflammation was noted upon treatment with antibody IM7, whose epitope lies outside the HA binding domain of CD44. Serum levels of sCD44 increased, and HA levels decreased, in response to IM7. KM201 and IM7 treatment reduced, but IRAWB14 treatment enhanced, the adhesion of leukocytes to HA. However, these antibodies had little effect on PG-specific immune responses. CONCLUSION: Each antibody acted in vivo by virtue of its combined effects on CD44-HA binding and CD44 shedding. The dramatic reduction in arthritis severity effected by IM7 treatment was associated with extensive shedding of cell surface CD44 molecules. Loss of CD44 appears to be a major factor in preventing CD44- and HA-dependent cell-matrix interactions at the inflammatory site. Our study indicates a critical role for CD44 in the pathology of joint inflammation and reveals a unique mechanism of receptor down-regulation, which can be used therapeutically.

7/3,AB/20 (Item 20 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

10178768 99156989 PMID: 10037799
LYVE-1, a new homologue of the CD44 glycoprotein, is a lymph-specific receptor for *hyaluronan*.
Banerji S; Ni J; Wang S X; Clasper S; Su J; Tammi R; Jones M; Jackson D G University of Oxford, Molecular Immunology Group, Nuffield Department of Medicine, John Radcliff Hospital, Headington, Oxford OX3 9DU, United Kingdom.
Journal of cell biology (UNITED STATES) Feb 22 1999, 144 (4) p789-801, ISSN 0021-9525 Journal Code: 0375356
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
The extracellular matrix glycosaminoglycan hyaluronan (HA) is an abundant component of skin and mesenchymal tissues where it facilitates cell migration during wound healing, inflammation, and embryonic morphogenesis. Both during normal tissue homeostasis and particularly after tissue injury, HA is mobilized from these sites through lymphatic vessels to the lymph nodes where it is degraded before entering the circulation for rapid uptake by the liver. Currently, however, the identities of HA binding molecules which control this pathway are unknown. Here we describe the first such molecule, LYVE-1, which we have identified as a major receptor for HA on the lymph vessel wall. The deduced amino acid sequence of LYVE-1 predicts a 322-residue type I integral membrane polypeptide 41% similar to the CD44 *HA* *receptor* with a 212-residue extracellular domain containing a single Link module the prototypic HA binding domain of the Link protein superfamily. Like CD44, the LYVE-1 molecule binds both soluble and immobilized HA. However, unlike CD44, the LYVE-1 molecule colocalizes with HA on the luminal face of the lymph vessel wall and is completely absent from blood vessels. Hence, LYVE-1 is the first lymph-specific *HA* *receptor* to be characterized and is a uniquely powerful marker for lymph vessels themselves.

7/3,AB/21 (Item 21 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

10175113 99159963 PMID: 10052598
Uptake of *hyaluronan* in hepatic metastases after blocking of liver endothelial cell receptors.
Mahteme H; Graf W; Larsson B S; Gustafson S
Department of Surgery, Uppsala University, Sweden.
Glycoconjugate journal (ENGLAND) Sep 1998, 15 (9) p935-9, ISSN 0282-0080 Journal Code: 8603310
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
To follow the biodistribution of exogenous hyaluronan in tumor-bearing animals, a total of seventeen inbred rats with hepatic metastases from a colonic adenocarcinoma received 125I-labelled hyaluronan by intravenous injections. Group I received only labeled hyaluronan (25 microg), whereas group II received 2.5 mg chondroitin sulphate prior to labeled hyaluronan, to block receptor uptake in normal liver endothelial cells. Animals in group III received intravenous, as well as intraperitoneal chondroitin sulphate (2.5 mg), to see if a better and prolonged blocking could be achieved. Radioactivity was visualized by whole body autoradiography, using phosphorimaging and the average radioactivity determined as phosphoimaging density units of the total area of hepatic metastases, normal liver, and skeletal muscle by computer-based image analysis. At 5 h, tumors in groups II and III showed higher uptake (4.8+/-1.8, P = .01 and 3.6+/-1.1, P = .01, respectively), in comparison to group I (1.8+/-0.6), and the mean normal liver/tumor concentration ratio was reduced from 21.4+/-10.1 in group I to 5.7+/-2.7 in group II and 3.5+/-1.1 in group III (P = .008 and P = .01, respectively). Our study shows that hyaluronan targets liver metastases of a colon adenocarcinoma. Furthermore, chondroitin sulphate pretreatment increases tumor uptake, while uptake at normal receptor sites is significantly reduced. The results also suggest that after blocking of normal hyaluronan/chondroitin sulphate receptors in healthy tissue, hyaluronan may be used to deliver drugs to specific *hyaluronan* *receptor*-positive sites of pathology.

7/3,AB/22 (Item 22 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

10133266 99107769 PMID: 9889313
Characterisation of the murine gene encoding the intracellular *hyaluronan* *receptor* IHABP (RHAMM).
Fieber C; Plug R; Sleeman J; Dall P; Ponta H; Hofmann M
Forschungszentrum Karlsruhe, Institute of Genetics, D-76021, Karlsruhe, Germany.
Gene (NETHERLANDS) Jan 8 1999, 226 (1) p41-50, ISSN 0378-1119 Journal Code: 7706761
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
We have recently shown that the published cDNA sequence encoding the murine cell surface receptor for hyaluronan-mediated motility (RHAMM) in fact represents a partial sequence of the cDNA encoding a new intracellular hyaluronic acid binding protein (IHABP). Here we publish the genomic organisation, including 700bp sequences of the promoter region, of the IHABP gene. The IHABP gene consists of 18 exons and spans more than 25kb. Part of the IHABP gene is identical with the published data on RHAMM. The IHABP gene apparently possesses one promoter region with one major transcriptional start point. IHABP is ubiquitously expressed at the mRNA and the protein level in all murine tissues, suggesting that the function of this intracellular hyaluronan binding protein is not restricted to migrating cells.

7/3,AB/23 (Item 23 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

10089876 99063528 PMID: 9848782
Hyaluronan induces monocyte chemoattractant protein-1 expression in renal tubular epithelial cells.
Beck-Schimmer B; Oertli B; Pasch T; Wuthrich R P
Physiological Institute, University of Zurich-Irchel, Zurich, Switzerland.
Journal of the American Society of Nephrology : JASN (UNITED STATES) Dec 1998, 9 (12) p2283-90, ISSN 1046-6673 Journal Code: 9013836 Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
Hyaluronan (HA) is a nonsulfated glycosaminoglycan that accumulates in the renal interstitium in immune-mediated kidney diseases. The functional significance of such HA deposition in the kidney has not been elucidated. Several studies have suggested that HA may exhibit proinflammatory effects. Since chemokines such as monocyte chemoattractant protein-1 (MCP-1) play an important role in the recruitment of leukocytes in renal injury, this study tested whether HA and its fragments could promote MCP-1 production by renal parenchymal cells. Mouse cortical tubular cells were stimulated with fragmented HA or with high molecular weight HA (Healon) in vitro and were examined for MCP-1 expression. Fragmented HA, but not Healon, increased MCP-1 mRNA within 30 min with a peak after 2 h. In addition, a 10-fold increase of MCP-1

protein in the supernatant was found after a 6-h stimulation with fragmented HA. The enhanced MCP-1 mRNA and protein expression in response to HA was dose-dependent between 1 and 100 microg/ml. Upregulation of MCP-1 protein production could be blocked by preincubation with actinomycin D or cycloheximide, suggesting that MCP-1 mRNA and protein expression in response to HA are based on de novo synthesis. The HA-stimulated MCP-1 production was also inhibited with anti-CD44 antibodies, suggesting that MCP-1 is upregulated at least in part by signaling through CD44. In summary, fragmented HA markedly stimulates renal tubular MCP-1 production by mechanisms that involve binding to the *HA* *receptor* CD44. It is hypothesized that the accumulation of HA in immune renal injury could participate in the recruitment and activation of inflammatory cells in vivo through production of MCP-1.

7/3,AB/24 (Item 24 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

10065095 99065413 PMID: 9850161
During human thymic development, beta 1 integrins regulate adhesion, motility, and the outcome of RHAMM/*hyaluronan* engagement. Gares S L; Giannakopoulos N; MacNeil D; Faull R J; Pilarski L M Department of Oncology and The Cross Cancer Institute, University of Alberta, Edmonton, Canada.
Journal of leukocyte biology (UNITED STATES) Dec 1998, 64 (6) p781-90, ISSN 0741-5400 Journal Code: 8405628
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
During human thymic differentiation, interactions between fibronectin (Fn)/beta1 integrins and hyaluronan (HA)/RHAMM control motility and Fn/beta1 integrins mediate spontaneous Fn-dependent adhesion. Multinegative (MN, CD3-4-8-) thymocytes exhibit strong spontaneous adherence to Fn (75%) that was efficiently inhibited by anti-alpha5beta1 and only weakly inhibited by anti-alpha4beta1. The relatively weak adherence of unfractionated thymocytes to Fn required both alpha4beta1 and alpha5beta1. Video time-lapse microscopy indicates that a subset of thymocytes also undergo spontaneous Fn-dependent motility mediated by alpha5beta1, alpha4beta1, and the *HA*-*receptor* RHAMM, but not by CD44. The loss of motility after hyaluronidase treatment of thymocytes indicated that motility is strongly dependent on HA. Of motile cells, 55% were DP, 19% were DN, and 24% were CD4+SP, but only 1% were CD8+SP. Overall, for MN thymocytes, beta1 integrin mediated Fn-adhesion, but after expression of CD4/CD8, beta1 integrins mediated Fn-dependent motility. Treatment with the activating anti-beta1 mAb QE.2E5 inhibited thymic motility and converted otherwise nonadherent thymocytes to an adherent state. High-avidity interactions via integrins appear to supercede the motogenicity of RHAMM and HA, suggesting that integrin avidity may regulate RHAMM. During thymic development, changes in adhesion or motility appear to be mediated by integrin avidity modulation.

7/3,AB/25 (Item 25 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

10053128 99040800 PMID: 9823466
Discrete domains within the *hyaluronan* *receptor* CD44 regulate membrane localization and cell migration.
Sheikh H; Legg J; Lewis C; Peck D; Isacke C
Department of Biology, Imperial College of Science, Technology and Medicine, London, UK.
Cell adhesion and communication (SWITZERLAND) 1998, 6 (2-3) p149-56, ISSN 1061-5385 Journal Code: 9417027
Document type: Journal Article; Review; Review, Tutorial
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
CD44 is the principle transmembrane receptor for the extracellular matrix glycosaminoglycan, hyaluronan. This receptor: ligand interaction is required for many normal cellular processes including lymphocyte homing into inflammatory sites, assembly of a pericellular matrix during chondrogenesis, wound healing and tissue morphogenesis during development. In order to mediate these diverse events, CD44 expressing cells must be able to regulate, and respond to, interactions with hyaluronan. The mechanisms responsible have been subject to scrutiny over the past few years as it has become clear that their disruption can underlie the progression of both metastatic tumours and chronic inflammatory diseases. Here we describe recent data identifying discrete regions within the transmembrane and cytoplasmic domains of CD44 which regulate this important adhesion receptor.

7/3,AB/26 (Item 26 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

10039237 99035780 PMID: 9818374
Hyaluronic *acid*-*receptor* binding demonstrated by synthetic adhesive proteoglycan peptide constructs and by cell receptors on the marine sponge Microciona prolifera.
Kuhns W J; Fernandez-Busquets X; Burger M M; Ho M; Turley E Marine Biological Laboratory, Woods Hole,

Massachusetts 02543, USA. Biological bulletin (UNITED STATES) Oct 1998, 195 (2) p216-8, ISSN 0006-3185 Journal Code: 2984727R
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed

7/3,AB/27 (Item 27 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

09935403 98355507 PMID: 9692758
The *hyaluronan* *receptor* RHAMM in noradrenergic fibers contributes to axon growth capacity of locus coeruleus neurons in an intraocular transplant model.
Nagy J I; Price M L; Staines W A; Lynn B D; Granholm A C Department of Physiology, Faculty of Medicine, University of Manitoba, Winnipeg, Canada.
Neuroscience (UNITED STATES) Sep 1998, 86 (1) p241-55, ISSN 0306-4522 Journal Code: 7605074
Contract/Grant No.: AG 12122; AG; NIA; MH 49661; MH; NIMH Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
The *hyaluronan* *receptor* for hyaluronic acid-mediated motility (RHAMM) plays a role in cell migration and motility in many systems. Recent observations on the involvement of RHAMM in neurite motility in vitro suggest that it might also be important in axon outgrowth in situ. This was addressed directly by investigating both RHAMM expression in the rat CNS and the ability of anti-RHAMM reagents to interfere with tissue growth and axon outgrowth in intraocular brainstem transplants. By western blotting, anti-RHAMM antibody detected a RHAMM isoform of 75,000 mol. wt in both whole brain homogenate and synaptosome preparations, and a 65,000 mol. wt isoform in synaptosomes. Immunofluorescence of adult brain sections revealed RHAMM-like immunoreactivity in varicose fibers that were also positive for the noradrenergic marker dopamine-beta-hydroxylase. Not all noradrenergic fibers contained RHAMM, nor was RHAMM detected in other monoaminergic fiber types. Lesions of noradrenergic fiber systems with beta-halobenzylamine-N-(2-chloroethyl)-N-ethyl-2-bromo benzylamine (DSP-4) eliminated RHAMM-positive fibers, but noradrenergic axons that sprouted extensively after this treatment were strongly RHAMM-positive. To assess RHAMM's role in fiber outgrowth, fetal brainstem tissue containing noradrenergic neurons was grafted into the anterior chamber of the eye. Treatment of grafts with anti-RHAMM antibody caused significant inhibition of tissue growth and axon outgrowth, as did a peptide corresponding to a hyaluronan binding domain of RHAMM. These agents had no such effects on transplants containing serotonergic and dopaminergic neurons. These results suggest that RHAMM, an extracellular matrix receptor previously shown to contribute to migratory and contact behavior of cells, may also be important in the growth and/or regenerative capacity of central noradrenergic fibers originating from the locus coeruleus.

7/3,AB/28 (Item 28 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

09935082 98357468 PMID: 9694095
Hyaluronan *receptor* expression increases in fetal excisional skin wounds and correlates with fibroplasia.
Lovvorn H N; Cass D L; Sylvester K G; Yang E Y; Crombleholme T M; Adzick N S; Savani R C
The Children's Institute for Surgical Science, The Children's Hospital of Philadelphia, The University of Pennsylvania School of Medicine, 19104, USA.
Journal of pediatric surgery (UNITED STATES) Jul 1998, 33 (7) p1062-9; discussion 1069-70, ISSN 0022-3468 Journal Code: 0052631 Contract/Grant No.: R01 HD25505; HD; NICHD
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
BACKGROUND/PURPOSE: The midgestation fetus heals incisional skin wounds scarlessly, whereas large excisional wounds scar. High concentrations of hyaluronan (HA) are associated with scarless fetal as opposed to scar-forming adult wound repair. Because expression of the HA receptors, CD44 and RHAMM (Receptor for HA-Mediated Motility), has been associated with adult wound fibroplasia, the authors postulated that fetal excisional wounds would show increased expression of CD44 and RHAMM as compared with incisional wounds. METHODS: Two models of fetal wound healing were examined. Fetal skin from human abortuses was heterotransplanted subcutaneously into severe combined immunodeficient (SCID) mice. Fourteen days after grafting, incisional or 2-mm excisional wounds were created (n = 6 per time-point). In addition, incisional and excisional (6 to 10 mm) wounds (n = 5 per time-point) were created on the backs of 70- to 75-day fetal lambs (term, 145 days). Tissue from both models was harvested at sequential time-points after injury. Wounds were studied histologically for fibroplasia and assayed for their HA content. CD44 and RHAMM expression were analyzed by immunohistochemistry and immunoblotting. RESULTS: As expected, in both models, incisional wounds healed scarlessly, whereas excisional wounds showed fibroplasia. Incisional

wounds of fetal lambs maintained a significantly higher HA content than excisional wounds 3 days after injury. Between 1 and 7 days in either human or sheep fetal wounds, immunostaining for CD44 and RHAMM markedly increased along the margins of excisional wounds as compared with incisional wounds and unwounded skin. Immunoblot analysis confirmed this increased *HA* *receptor* expression in both models. CONCLUSIONS: *HA* *receptor* expression increased in both human and sheep fetal excisional wounds and correlated with fibroplasia and a reduced HA content. The authors speculate that strategies to limit the expression or function of HA receptors during postnatal wound repair may modify the development of scar.

7/3,AB/29 (Item 29 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

09921900 98371558 PMID: 9698509
Inhibiting the differentiation of myocardiocytes by *hyaluronic* acid.
Iocono J A; Bisignani G J; Krummel T M; Ehrlich H P
Department of Surgery, Milton S. Hershey Medical Center, College of Medicine, Hershey, Pennsylvania 17033, USA.
Journal of surgical research (UNITED STATES) May 1998, 76 (2) p111-6 , ISSN 0022-4804 Journal Code: 0376340
Contract/Grant No.: GM17566; GM; NIGMS; RO1 GM 41343; GM; NIGMS Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
BACKGROUND: In vitro experimentation found that wounded midgestation fetal mouse hearts heal scarlessly. Scarless repair occurs in an environment enriched in hyaluronic acid (HA), while in the absence of HA and the inclusion of hyaluronidase (HAdase), repair by scarring occurs. Excess HA downregulates the expression of the specific *HA* *receptor* , RHAMM (receptor for HA-mediated motility). The expression of RHAMM and the migration of cardiac cells from fetal heart explants were investigated in the presence of excess HA and added HAdase. METHOD: Hearts from Gestational Day 15 fetal mice (term = 20) were cut into four fragments, established as explant cultures, and assigned to one of three treatment groups: 400 micrograms/ml HA, 50 U/ml HAdase, or saline. Cellular outgrow was recorded at Day 7. The character of the migrating cells (fibroblast-like or myocardiocyte) was determined by immunostaining for filamentous actin (f-actin, microfilaments) or desmin (intermediate filaments). The expression of RHAMM was documented also. RESULTS: The inclusions of HA stimulated cell migration and proliferation, perpetuated cells as immature myocardiocytes, and blocked the expression of RHAMM. The inclusion of HAdase limited cell migration and proliferation, promoted the differentiation of cells into myocardiocytes, and increased the number of cells expressing RHAMM. CONCLUSION: Increased concentrations of HA promoted the proliferation and migration of an immature population of myocardiocytes. On the other hand the inclusion of HAdase inhibits the migration and proliferation of cells and promotes the appearance of myocardiocytes with a fibroblast-like morphology. The speculation is that excess HA may promote proliferation and migration of immature myocardiocytes into a heart defect, leading to replacement of lost myocardium with contractile tissue rather than dysfunctional scar.

7/3,AB/30 (Item 30 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

09886998 98326735 PMID: 9663602
Inhibition of tumor growth in vivo by *hyaluronan* oligomers. Zeng C; Toole B P; Kinney S D; Kuo J W; Stamenkovic I
Department of Pathology, Harvard Medical School, and Pathology Research Laboratories, Massachusetts General Hospital, Boston 02129, USA. International journal of cancer. Journal international du cancer (UNITED STATES) Jul 29 1998, 77 (3) p396-401, ISSN 0020-7136 Journal Code: 0042124
Contract/Grant No.: CA05838; CA; NCI; CA55735; CA; NCI; HD23681; HD; NICHD
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
One of the critical events in tumor growth and metastasis is the interaction between tumor cells and host tissue stroma, mediated by different adhesion receptor repertoires in different tumor cell types. Several lines of evidence indicate that interaction between the *hyaluronan* *receptor* CD44, expressed on tumor cells, and host tissue stromal hyaluronan can enhance growth and invasiveness of certain tumors. Disruption of CD44-hyaluronan interaction by soluble recombinant CD44 has been shown to inhibit tumor formation by lymphoma and melanoma cells transfected with CD44. Since hyaluronan is a ubiquitous glycosaminoglycan polymer from which oligosaccharides of defined size can be readily purified, we tested the ability of hyaluronan oligomers to inhibit tumor formation by subcutaneously (s.c.) injected B16F10 melanoma cells. Our results indicate that hyaluronan oligomers injected at concentrations as low as 1 mg/ml can markedly inhibit B16F10 melanoma growth, providing a potentially attractive reagent for the control of local tumor development.

7/3,AB/31 (Item 31 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

09879209 98301769 PMID: 9637922
Identification and functional analysis of the ezrin-binding site in the *hyaluronan* *receptor*, CD44.
Legg J W; Isacke C M
Department of Biology, Imperial College of Science, Technology and Medicine, London, UK.
Current biology : CB (ENGLAND) Jun 4 1998, 8 (12) p705-8, ISSN 0960-9822 Journal Code: 9107782
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
ERM (ezrin, radixin and moesin) proteins function as linkers between the actin cytoskeleton and the plasma membrane. In addition to this structural role, these proteins are highly regulatable making them ideal candidates to mediate important physiological events such as adhesion and membrane morphology and to control formation and breakdown of membrane-cytoskeletal junctions. Recently, a direct interaction in vitro has been demonstrated between ERM proteins and the *hyaluronan* *receptor*, CD44. We have mapped the ezrin-binding site to two clusters of basic amino acids in a membrane-proximal 9 amino-acid region within the CD44 cytoplasmic domain. To investigate the functional importance of this interaction in vivo, we created a number of mutations within full-length CD44 and expressed these mutants in human melanoma cells. We demonstrate here that mutations within the ezrin-binding site do not disrupt the plasma membrane localization of CD44 and, in addition, that this region is not required to mediate efficient hyaluronan binding. These studies suggest that ERM proteins mediate the outside-in, rather than inside-out, signalling of adhesion receptors.

7/3,AB/32 (Item 32 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

09849714 98264864 PMID: 9601098
The human *hyaluronan* *receptor* RHAMM is expressed as an intracellular protein in breast cancer cells.
Assmann V; Marshall J F; Fieber C; Hofmann M; Hart I R
Richard Dimbleby Department of Cancer Research/ICRF Laboratory, St Thomas' Hospital, Lambeth Palace Road, London SE1 7EH, UK. v.assmann@icrf.icnet.uk
Journal of cell science (ENGLAND) Jun 1998, 111 (Pt 12) p1685-94, ISSN 0021-9533 Journal Code: 0052457
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
The receptor for hyaluronan mediated motility (RHAMM) has been reported to mediate migration, transformation, and metastatic spread of murine fibroblasts. Here we describe the expression of two human RHAMM isoforms, which are generated by alternative splicing of the primary gene transcript, by a series of human breast carcinoma cell lines. A polyclonal antibody, raised against a bacterially expressed RHAMM fusion protein, detected an 85-90 kDa protein by western blot analysis. No correlation between the level of RHAMM mRNA and protein expression with known metastatic/malignant potential of the tumour cell lines was observed. Interestingly, we found that the antibody did not stain the cell surface but the cytoplasm of breast cancer cells. The intracellular localisation of RHAMM was confirmed by subcellular fractionation studies. RHAMM proteins were capable of binding to hyaluronan, but not to heparin or chondroitin sulphate, in an vitro binding assay. We also provide evidence that a potential hyaluronan-binding motif in the N terminus of the protein is not involved in the interaction of RHAMM with hyaluronan. Our findings lead us to conclude that RHAMM does not function as a conventional motility receptor for HA in human breast cancer cells and we suggest the term RHAMM be substituted by 'intracellular hyaluronic acid binding protein' (IHABP).

7/3,AB/33 (Item 33 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

09803755 98225222 PMID: 9556628
The *hyaluronan* *receptor* RHAMM regulates extracellular-regulated kinase.
Zhang S; Chang M C; Zylka D; Turley S; Harrison R; Turley E A Hospital for Sick Children, Division of Cardiovascular Research, Toronto, Ontario, Canada M5G1X8.
Journal of biological chemistry (UNITED STATES) May 1 1998, 273 (18) p11342-8, ISSN 0021-9258 Journal Code: 2985121R
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
We have identified two RHAMM (receptor for hyaluronan-mediated motility) isoforms that encode an alternatively spliced exon 4 (Hall, C. L., Yang, B., Yang, X., Zhang, S., Turley, M., Samuel, S., Lange, L. A., Wang, C., Curpen, G. D., Savani, R. C., Greenberg, A. H., and Turley, E. A. (1995) Cell 82, 19-26 and Wang, C., Entwistle, J., Hou, G., Li, Q., and Turley, E. A. (1996) Gene 174, 299-306). One of these, RHAMM variant 4

(RHAMMv4), is transforming when overexpressed and regulates Ras signaling (Hall et al.). Here we note using flow cytometry and confocal analysis that RHAMM isoforms encoding exon 4 occur both on the cell surface and in the cytoplasm. Epitope-tagging experiments indicate that RHAMMv4 occurs only in the cytoplasm. Several observations suggest that both cell surface RHAMM isoforms and RHAMMv4 are involved in regulating extracellular-regulated kinase (ERK) activity. Affinity-purified anti-RHAMM exon 4 antibodies block the ability of platelet-derived growth factor to activate ERK, and these reagents modify the protein tyrosine phosphorylation profile of proteins resulting from treatment with platelet-derived growth factor. A dominant negative form of RHAMMv4 inhibits mutant active Ras activation of ERK and coimmunoprecipitates with both mitogen-activated protein kinase kinase and ERK, suggesting that the intracellular RHAMMv4 acts downstream of Ras, possibly at the level of mitogen-activated protein kinase kinase-ERK interactions. Consistent with this, overexpression of RHAMMv4 constitutively activates ERK. These results identify a novel mechanism for the regulation of the Ras-ERK signaling pathway and suggest that RHAMM plays multiple roles in this regulation.

7/3,AB/34 (Item 34 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

09753971 98170173 PMID: 9509434
Characterization of CD44-mediated *hyaluronan* binding by renal tubular epithelial cells.
Oertli B; Fan X; Wuthrich R P
Physiological Institute, University of Zurich-Irchel, Switzerland. Nephrology, dialysis, transplantation : official publication of the European Dialysis and Transplant Association - European Renal Association (ENGLAND) Feb 1998, 13 (2) p271-8, ISSN 0931-0509 Journal Code: 8706402
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
BACKGROUND: CD44 is the main receptor for the extracellular polysaccharide hyaluronan (HA). We have recently shown that CD44 is strongly induced on renal tubular epithelial cells (TEC) in autoimmune renal injury and that HA accumulates in the renal interstitium (Kidney Int 1996; 50: 156-163 and Nephrol Dial Transplant 1997; 12: 1344-1353). The functional significance of enhanced tubular CD44 expression and its interaction with HA are not known. The purpose of the present study was to characterize renal tubular CD44 expression and CD44-mediated HA binding in vitro and to investigate the growth modulating effects in response to HA binding by TEC. METHODS: RT-PCR analysis, flow cytometry, confocal microscopy and Western blotting were used to examine cell surface and soluble CD44 expression by cultured TEC, using SV40-transformed mouse cortical tubular (MCT) cells. HA binding characteristics were examined by flow cytometry and effects of HA on TEC cell growth by [3H]thymidine incorporation. RESULTS: By RT-PCR analysis MCT cells expressed predominantly the standard form of CD44 mRNA, whereas the expression of variant forms was very weak. Confocal microscopy showed that CD44 was expressed basolaterally and apically on MCT cells with strong staining on microvilli. Shedding of CD44 from MCT cells could be induced with crosslinking of anti-CD44 mAbs or with PMA stimulation. MCT cells constitutively bound HA and this binding could be modulated with anti-CD44 mAbs. Soluble and plate-bound HA markedly inhibited MCT cell growth. CONCLUSIONS: CD44 is a regulated *HA* *receptor* on MCT cells which can be shed into the cellular environment. Upon binding of HA, CD44 functions as a growth inhibitory cell surface protein in MCT cells. We speculate that the interaction of CD44 with HA may have important regulatory effects on cell proliferation in tubulointerstitial renal diseases.

7/3,AB/35 (Item 35 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

09698080 98114484 PMID: 9446831
Ultrastructural analysis of human epidermal CD44 reveals preferential distribution on plasma membrane domains facing the *hyaluronan*-rich matrix pouches.
Tuhkanen A L; Tammi M; Pelttari A; Agren U M; Tammi R
Department of Anatomy, University of Kuopio, Kuopio, Finland. journal of histochemistry and cytochemistry : official journal of the Histochemistry Society (UNITED STATES) Feb 1998, 46 (2) p241-8, ISSN 0022-1554 Journal Code: 9815334
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
We used immunogold staining and stereology to examine the ultrastructural localization and to estimate the relative content of CD44 in different strata and cell types of normal human epidermis. We found that CD44 existed almost exclusively on the plasma membranes; only rare labeling occurred on vesicular structures within the cytoplasm. Quantitation of the immunogold particles indicated that the labeling density of melanocytes corresponded to that of basal keratinocytes, and Langerhans cells displayed a labeling density of approximately 10% that of the surrounding spinous cells. Among keratinocyte strata, the highest labeling

density occurred on spinous cells, suggesting upregulation of CD44 after detachment from the basement membrane. The plasma membrane distribution of CD44 was compartmentalized, with little signal on cell-cell and cell-substratum contact sites such as desmosomes, the plasma membrane domain facing the basement membrane, and the close apposition of terminally differentiating granular cells. In contrast, CD44 was abundant on plasma membrane domains facing an open intercellular space, rich in hyaluronan. This distribution is in line with a role of CD44 as a *hyaluronan* *receptor*, important in the maintenance of the intercellular space for nutritional and cell motility functions in stratified epithelia.

7/3,AB/36 (Item 36 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

09501911 97393251 PMID: 9249768
Upregulated renal tubular CD44, *hyaluronan*, and osteopontin in kdkd mice with interstitial nephritis.
Sibalic V; Fan X; Loffing J; Wuthrich R P
Institute of Physiology, University of Zurich-Irchel, Switzerland. Nephrology, dialysis, transplantation : official publication of the European Dialysis and Transplant Association - European Renal Association (ENGLAND) Jul 1997, 12 (7) p1344-53, ISSN 0931-0509 Journal Code: 8706402
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
BACKGROUND: The hyaluronan (*HA*) *receptor* CD44 is upregulated on parenchymal cells in various inflammatory lesions and could play a role in immune injury. The purpose of the present study was to examine CD44 and its ligands HA and osteopontin (Opn) in a murine model of tubulointerstitial nephritis (TIN). METHODS: The expression of CD44 was investigated by immunofluorescence staining and RNA analysis in kidneys of kdkd mice with autoimmune TIN. The CD44 expression was then correlated with the location of its ligands HA and Opn. RESULTS: CD44 is expressed de novo by tubular epithelial cells (TEC) in areas of tubular injury in kdkd kidneys, but not in normal control kidneys. CD44 positive lymphocytes and macrophages also infiltrate the kidney to kdkd mice. RT-PCR and Southern blot analysis demonstrate that transcripts encoding standard and variant forms of CD44 are increased in kdkd mice with TIN. In parallel the CD44 ligand HA also accumulates in kdkd kidneys in the interstitial space, particularly in cortical areas of tubular injury. Furthermore, the expression of the chemotactic protein Open is enhanced in kdkd kidney, predominantly in areas of tubular injury. Opn mRNA expression also increases markedly in kdkd kidneys compared with normal kidneys, and correlates with disease severity. CONCLUSIONS: Prominent CD44 expression by TEC in areas of tubulointerstitial lesions is a characteristic feature of kdkd mice. The de novo appearance of CD44 on injured TEC might allow interaction with the ligands HA and Opn in vivo. Interaction of CD44 with these ligands could participate in the tubulointerstitial inflammatory response in kdkd mice.

7/3,AB/37 (Item 37 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

09495218 97407336 PMID: 9260569
Is serum *hyaluronan* a helpful tool in the management of patients with liver diseases?
Lindqvist U
Department of Internal Medicine, University Hospital, Uppsala, Sweden. Journal of internal medicine (ENGLAND) Jul 1997, 242 (1) p67-71, ISSN 0954-6820 Journal Code: 8904841
Document type: Journal Article; Review; Review, Tutorial
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
The results of serial determinations of serum hyaluronan indicate a prognostic value in progressive liver damage. In primary biliary cirrhosis and in cirrhotic alcoholic liver diseases serum hyaluronan level discriminates between early and advanced disease. In alcoholic liver disease serum hyaluronan can be applied as assessment of haemodynamic changes. Serum hyaluronan is of use as a non-invasive index of liver fibrosis in chronic viral hepatitis. A reversible defect in the *hyaluronan* *receptor* of the hepatic endothelial cells was suggested following studies on paracetamol-induced acute liver damage. In liver transplantation, graft function can be predicted by determination of the venous effluent of hyaluronan.

7/3,AB/38 (Item 38 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

09460420 97337999 PMID: 9194670
The role of *hyaluronic* acid as a mediator and regulator of cervical ripening.
El Maradny E; Kanayama N; Kobayashi H; Hossain B; Khatun S; Liping S; Kobayashi T; Terao T
Department of Obstetrics and Gynecology, Hamamatsu University School of Medicine, Handa-cho, Japan.
Human reproduction (Oxford, England) (ENGLAND) May 1997, 12 (5) p1080-8, ISSN 0268-1161 Journal Code: 8701199
Document type: Journal Article

Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
During pregnancy, hyaluronic acid (HA) concentration in the human cervix is very low, but increases rapidly at the onset of labour. HA has a high affinity for water molecules and hence can maintain tissue hydration. HA can stimulate collagenase production in rabbit cervix, and also stimulates migration and function of polymorphonuclear leukocytes in the tissues. It is an endogenous regulator of interleukin-i (IL-i). We hypothesized that HA plays an essential role during cervical ripening. The effect of exogenous application of HA (20 mg) on non-pregnant and pregnant (day 23) rabbit cervices was compared with controls. HA induced cervical ripening in both pregnant and non-pregnant animals, and cervical water content was significantly increased. Tissue collagen was markedly decreased. The localization and distribution of HA and *HA* *receptor* CD44 was determined in non-pregnant and pregnant human cervical connective tissue using biotinylated HA binding protein and CD44 monoclonal antibodies. Both were widely distributed in the connective tissues, especially around the blood vessels and cervical glands. The effect of IL-8 (50, 100, 150 and 200 ng/ml) on HA production and hyaluronidase (HAase) activity was investigated in cultures of lower uterine segment collected during elective Caesarean sections. HA production was stimulated in a dose-dependent manner; there was no effect on hyaluronidase activity. HA administration (0.5, 1 and 2 mg/ml) stimulated the activities of collagenase and gelatinase together with IL-8 production in the culture supernatants. Thus HA may play an important role in cervical ripening, being involved in the regulation of cervical tissue water content, collagenolytic enzymes and cytokines.

7/3,AB/39 (Item 39 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

09442540 97344865 PMID: 9201232
Avian influenza A viruses differ from human viruses by recognition of sialyloligosaccharides and gangliosides and by a higher conservation of the *HA* *receptor*-binding site.
Matrosovich M N; Gambaryan A S; Teneberg S; Piskarev V E; Yamnikova S S; Lvov D K; Robertson J S; Karlsson K A
M. P. Chumakov Institute of Poliomyelitis and Viral Encephalitides, Russian Academy of Medical Sciences, Moscow, Russia.
Virology (UNITED STATES) Jun 23 1997, 233 (1) p224-34, ISSN 0042-6822 Journal Code: 0110674
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
Avian influenza virus strains representing most hemagglutinin (HA) subtypes were compared with human influenza A (H1N1,H3N2) and B virus isolates, including those with no history of passaging in embryonated hen's eggs, for their ability to bind free N-acetylneuraminic acid (Neu5Ac) and sialyllollgosaccharides in a competitive binding assay and to attach to gangliosides in a solid-phase adsorption assay. The avian viruses, irrespective of their HA subtype, showed a higher affinity for sialyl-3-lactose and the other Neu5Ac2-3Gal-terminated oligosaccharides and a lower affinity for sialyl-6-lactose than for free Neu5Ac, indicative of specific interactions between the HA and the 3-linked Gal and poor accommodation of 6-linked Gal in the avian receptor-binding site (RBS). Human H1 and H3 strains, by contrast, were unable to bind to 3-linked Gal, interacting instead with the asialic portion of sialyl-6-(N-acetyllactosamine). Different parts of this moiety were recognized by H3 and H1 subtype viruses (Gal and GlcNAc, respectively). Comparison of the HA amino acid sequences revealed that residues in positions. 138, 190, 194, 225, 226, and 228 are conserved in the avian RBS, while the human HAs harbor substitutions at these positions. A characteristic feature of avian viruses was their binding to Neu5Ac2-3Gal-containing gangliosides. This property of avian precursor viruses was preserved in early human H3 isolates, but was gradually lost with further circulation of the H3 HA in humans. Consequently, later human H3 isolates, as well as H1 and type B human strains, were unable to bind to short Neu5Ac2-3Gal-terminated gangliosides, an incompatibility that correlated with higher glycosylation of the HA globular head of human viruses. Our results suggest that the RBS is highly conserved among HA subtypes of avian influenza virus, while that of human viruses displays distinctive genotypic and phenotypic variability.

7/3,AB/40 (Item 40 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

09434778 97339888 PMID: 9196442
Glioma invasion in vitro is mediated by CD44-*hyaluronan* interactions.
Radotra B; McCormick D
Neuro-Oncology Laboratory, Queen's University of Belfast, U.K. Journal of pathology (ENGLAND) Apr 1997, 181 (4) p434-8, ISSN 0022-3417 Journal Code: 0204634
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed

Invasion is a clinically important problem contributing to mortality and morbidity in patients with gliomas, but the mechanism(s) by which glioma cells invade surrounding brain structures is poorly understood. Various experimental models have been used in attempts to elucidate the process of glioma invasion. An in vitro model which is increasingly being employed involves measurement of the rate of invasion of tumour cells through Matrigel-a complex mixture of extracellular matrix components derived from the Engelbroth-Holm-Swarm (EHS) sarcoma. This model has been used to examine the possibility that extracellular hyaluronan (HA) might facilitate the invasive behaviour of human glioma cells. The major component of Matrigel is laminin, with smaller amounts of collagen IV, heparan sulphate proteoglycans, entactin, and nidogen but it lacks HA. In our experiments, we have incorporated HA into Matrigel and have measured its effect on the rate of invasion of human glioma cells in a modified Boyden chamber assay system. The incorporation of HA (50-800 mg/cm2) resulted in a dose-dependent increase in invasion. Invasion was enhanced by up to 70 per cent in comparison with HA-free Matrigel. Since CD44 is a major *HA* *receptor* expressed on gliomas, it might have a role in the HA-mediated facilitation of invasion. This was tested by blocking CD44 with specific antibody, which resulted in a 43 per cent reduction in invasion rate. We conclude that in an in vitro model system, HA enhances invasion of glioma cells and that the mechanism involves a CD44-HA interaction.

7/3,AB/41 (Item 41 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

09332922 97214995 PMID: 9061360
Identification of a 175 kDa protein as the ligand-binding subunit of the rat liver sinusoidal endothelial cell *hyaluronan* *receptor*.
Yannariello-Brown J; Zhou B; Weigel P H
Department of Biochemistry and Molecular Biology, University of Oklahoma Health Sciences Center, Oklahoma City 73190, USA.
Glycobiology (ENGLAND) Feb 1997, 7 (1) p15-21, ISSN 0959-6658 Journal Code: 9104124
Contract/Grant No.: GM35978; GM; NIGMS
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
The rat liver sinusoidal endothelial cell (LEC) hyaluronan (*HA*) *receptor* was previously identified using a photoaffinity HA derivative (J. Biol. Chem., 267, 20451-20456, 1992). Two polypeptides with M(r) = 175,000 and 166,000, were consistently crosslinked, suggesting that the LEC *HA* *receptor* is an oligomer. Whether one or both subunits participate in HA binding, was not determined. Here we investigate the HA-subunit interactions and the potential oligomeric nature of the LEC *HA* *receptor* . When Sephacryl-400 gel filtration chromatography was used to enrich the *HA* *receptor*, the 175 kDa polypeptide was the major band seen by SDS-PAGE analysis. Little staining was seen at 166 kDa, suggesting that the 175 kDa protein could be separated from the 166 kDa protein and still retain HA-binding activity. A ligand blot assay was used to determine if each individual subunit could bind HA. LEC proteins were separated by nonreducing SDS-PAGE, and then immobilized onto nitrocellulose. 125I-HA bound to a 175 kDa polypeptide but not to the 166 kDa protein. A high molecular weight band of approximately 300,000 also bound 125I-HA. 125I-HA binding to the 175 and 300 kDa proteins showed the same specificity of competition with a panel of carbohydrates as the bona fide LEC *HA* *receptor* . The 175 kDa HA-binding subunit may be nonglobular (asymmetric), since its apparent size by SDS-PAGE is dependent on the polyacrylamide gel pore size; M(r) increases as porosity decreases. LECs were crosslinked to an 125I-labeled photoaffinity HA derivative and the HA saccharides were then released with hyaluronidase. After SDS-PAGE without reduction, radiolabeled bands were seen at 175 and 166 kDa (3:1 ratio), and a high MW (approximately 300,000) species was also detected. These data support an oligomeric model of the LEC *HA* *receptor*, and show that the 175 kDa protein possesses HA-binding activity independent from the 166 kDa polypeptide.

7/3,AB/42 (Item 42 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

09323328 97238717 PMID: 9102228
Absence of functional CD44 *hyaluronan* *receptor* on human NMYC-amplified neuroblastoma cells.
Gross N; Balmas K; Brognara C B
Onco-hematology Unit, University Hospital, Lausanne, Switzerland. Cancer research (UNITED STATES) Apr 1 1997, 57 (7) p1387-93, ISSN 0008-5472 Journal Code: 2984705R
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
CD44 represents a heterogeneous group of surface glycoproteins, involved in cell-cell and cell-matrix interactions. CD44 is the major receptor for hyaluronate (HA), a component of cell matrices, and most of CD44 known functions are attributed to its ability to recognize HA. We have recently shown that although a majority of human neuroblastomas (NBs), a childhood

cancer, express high levels of CD44H, high stages and tumors with amplification of the NMYC proto-oncogene fail to express CD44. Lack of CD44 expression is strongly associated with the presence of NMYC amplification and has been further shown to represent a new feature for predicting risk of disease progression and dissemination. In the present study, we have investigated the role of CD44 expressed by NB cell lines and the possible relationship among the presence of NMYC amplification, functional expression of CD44 receptor, and tumorigenic properties of NB cells. A panel of cell lines with variable NMYC amplification and/or overexpression, as well as clonal and stable NMYC-transfected NB cells, were analyzed for CD44 expression and ability to bind HA. Our results confirmed previous observations that in NB cell lines lack of CD44 is not always related to the presence of NMYC amplification, with a number of cell lines or transfectants with both CD44 expression and NMYC amplification. However, the ability of the CD44 receptor to bind immobilized hyaluronan was restricted to CD44H+ cell lines without NMYC amplification (SH-EP and ACN). The HA-binding function was CD44 dependent and could be specifically blocked by an anti-CD44 antibody. No induction of functional HA binding was obtained with NMYC-amplified cell lines or NMYC transfectants, despite an induced increase of CD44 expression upon differentiation or after tentative activation of the receptor with phorbol esters. Inhibition of N-linked glycosylation with tunicamycin resulted in decreased HA binding of cells bearing an active CD44 receptor. We conclude that NMYC-amplified NB cell lines either do not express CD44 at all or express a nonfunctional receptor, whereas nonamplified cells constitutively express an active receptor. The lack of functional HA binding in NB cells might be partly due to incomplete N-glycosylation. The involvement of NMYC in the regulation of N-linked glycosylation can be suspected.

7/3,AB/43 (Item 43 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

09269126 97154532 PMID: 9001250
AP-1-mediated invasion requires increased expression of the *hyaluronan* *receptor* CD44.
Lamb R F; Hennigan R F; Turnbull K; Katsanakis K D; MacKenzie E D; Birnie G D; Ozanne B W
CRC Beatson Laboratories, Beatson Institute for Cancer Research, Bearsden, Glasgow, Scotland.
Molecular and cellular biology (UNITED STATES) Feb 1997, 17 (2) p963-76, ISSN 0270-7306 Journal Code: 8109087
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
Fibroblasts transformed by Fos oncogenes display increased expression of a number of genes implicated in tumor cell invasion and metastasis. In contrast to normal 208F rat fibroblasts, Fos-transformed 208F fibroblasts are growth factor independent for invasion. We demonstrate that invasion of v-Fos- or epidermal growth factor (EGF)-transformed cells requires AP-1 activity. v-Fos-transformed cell invasion is inhibited by c-jun antisense oligonucleotides and by expression of a c-jun dominant negative mutant, TAM-67. EGF-induced invasion is inhibited by both c-fos and c-jun antisense oligonucleotides. CD44s, the standard form of a transmembrane receptor for hyaluronan, is implicated in tumor cell invasion and metastasis. We demonstrate that increased expression of CD44 in Fos- and EGF-transformed cells is dependent upon AP-1. CD44 antisense oligonucleotides reduce expression of CD44 in v-Fos- or EGF-transformed cells and inhibit invasion but not migration. Expression of a fusion protein between human CD44s and Aequorea victoria green fluorescent protein (GFP) in 208F cells complements the inhibition of invasion by the rat-specific CD44 antisense oligonucleotide. We further show that both v-Fos and EGF transformations result in a concentration of endogenous CD44 or exogenous CD44-GFP at the ends of pseudopodial cell extensions. These results support the hypothesis that one role of AP-1 in transformation is to activate a multigenic invasion program.

7/3,AB/44 (Item 44 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

09206721 97096814 PMID: 8941660
Hyaluronan (*HA*) fragments induce chemokine gene expression in alveolar macrophages. The role of *HA* size and CD44.
McKee C M; Penno M B; Cowman M; Burdick M D; Strieter R M; Bao C; Noble P W
Department of Medicine, Johns Hopkins University School of Medicine, Baltimore, Maryland 21205, USA.
Journal of clinical investigation (UNITED STATES) Nov 15 1996, 98 (10) p2403-13, ISSN 0021-9738 Journal Code: 7802877
Contract/Grant No.: K11HL02880; HL; NHLBI
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
Hyaluronan (HA) is a glycosaminoglycan constituent of extracellular matrix. In its native form HA exists as a high molecular weight polymer, but during inflammation lower molecular weight fragments accumulate. We have identified a collection of inflammatory genes induced in

macrophages by HA fragments but not by high molecular weight HA. These include several members of the chemokine gene family: macrophage inflammatory protein-1alpha, macrophage inflammatory protein-1beta, cytokine responsive gene-2, monocyte chemoattractant protein-1, and regulated on activation, normal T cell expressed and secreted. HA fragments as small as hexamers are capable of inducing expression of these genes in a mouse alveolar macrophage cell line, and monoclonal antibody to the *HA* *receptor* CD44 completely blocks binding of fluorescein-labeled HA to these cells and significantly inhibits HA-induced gene expression. We also investigated the ability of HA fragments to induce chemokine gene expression in human alveolar macrophages from patients with idiopathic pulmonary fibrosis and found that interleukin-8 mRNA is markedly induced. These data support the hypothesis that HA fragments generated during inflammation induce the expression of macrophage genes which are important in the development and maintenance of the inflammatory response.

7/3,AB/45 (Item 45 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

09182297 97083995 PMID: 8930339
Evidence for receptors for *hyaluronan* in discrete nerve cell populations of the brain.
Fuxe K; Agnati L F; Tinner B; Forsberg N; McCourt P; Gustafson S Department of Neuroscience, Karolinska Institutet, Stockholm, Sweden. Brain research (NETHERLANDS) Oct 14 1996, 736 (1-2) p329-37, ISSN 0006-8993 Journal Code: 0045503
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
Evidence is presented, based on immunoblotting, immunohistochemistry and double immunolabelling procedures, for the existence of *hyaluronan* *receptor* immunoreactivity in discrete nerve cell populations of the rat brain, present within the zona compacta and the zona reticulata of the substantia nigra, the ventral tegmental area the locus coeruleus, the mesencephalic trigeminal nucleus, the nucleus of the trapezoid body, the motor trigeminal nucleus and the lateral cerebellar nucleus. With preimmune serum control, this *hyaluronan* *receptor* immunoreactivity could not be demonstrated. Double immunofluorescence immunocytochemistry, using a well-characterized *hyaluronan* *receptor* antiserum, together with the tyrosine hydroxylase antiserum, in the presence or absence of detergent, demonstrated the existence of *hyaluronan* *receptor* immunoreactivity in dopamine nerve cells of the substantia nigra and the ventral tegmental area and in noradrenaline nerve cells of the locus coeruleus, previously shown not to stain for hyaluronan. In all the nerve cells, the immunoreactivity had the appearance of punctate bodies mainly located in the cytoplasm of the perikarya of the above nerve cell populations as also shown by confocal laser microscopy in the mesencephalic trigeminal nucleus. Based on these observations, it is concluded that hyaluronan receptors exist in discrete nerve cell populations of the brain, including many noradrenaline and dopamine neurones. In all nerve cells, it is located intracellularly in bodies possibly representing clustered hyaluronan receptors undergoing endocytosis. The results open up the possibility that hyaluronan receptors may reduce high concentrations of hyaluronic acid in the surrounding matrix, thereby facilitating communication between adjacent neurones. Intracytoplasmatic hyaluronic acid may also be of special importance for neuronal plasticity, in view of the ability of hyaluronic acid to activate protein kinase activity and/or by influencing the architecture of the cytoskeleton.

7/3,AB/46 (Item 46 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

09164975 97069734 PMID: 8912714
CD44-anchored *hyaluronan* -rich pericellular matrices: an ultrastructural and biochemical analysis.
Knudson W; Aguiar D J; Hua Q; Knudson C B
Department of Biochemistry, Rush Medical College, Rush-Presbyterian-St. Luke's Medical Center, Chicago, Illinois 60612-3864, USA.
Experimental cell research (UNITED STATES) Nov 1 1996, 228 (2) p216-28, ISSN 0014-4827 Journal Code: 0373226
Contract/Grant No.: AR39239; AR; NIAMS; AR39507; AR; NIAMS Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
The chondrocyte pericellular matrix is an essential zone for cartilage matrix assembly and turnover. Electron micrographs of native endogenous and composition-defined exogenous pericellular matrices, both preserved via ruthenium hexaminetrichloride fixation procedures, depict strikingly similar networks of hyaluronan and proteoglycan extending out from the cell surface. Biochemical and morphological analyses of matrix regrowth show that monoclonal antibodies directed against the *hyaluronan* *receptor* CD44 blocked chondrocyte pericellular matrix assembly. Immunoperoxidase electron microscopy was used to display regular repeating spacing patterns of hyaluronan/proteoglycan assembly at the cell surface. These patterns compared well with the ultrastructural

immunolocalization of CD44 at the cell surface. All of these data suggest that the *hyaluronan* *receptor* CD44 retains and participates in the assembly of the chondrocyte pericellular matrix.

7/3,AB/47 (Item 47 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

09153946 97052119 PMID: 8896754
Hyaluronic acid induced *hyaluronic* acid binding protein phosphorylation and inositol triphosphate formation in lymphocytes. Rao C M; Deb T B; Datta K
Biochemistry Laboratory, School of Environmental Sciences, Jawaharlal Nehru University, New Delhi, India.
Biochemistry and molecular biology international (AUSTRALIA) Oct 1996, 40 (2) p327-37, ISSN 1039-9712 Journal Code: 9306673 Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
In this report, the role of 34 kDa HA-binding protein in hyaluronic acid-induced cellular signalling in lymphocytes has been examined. The binding of 125I-HA to lymphocytes in vivo was found to be inhibited by pre-incubation of the cells with anti-34 kDa HA-binding protein antibodies, thus confirming 34 kDa HA-binding protein as the specific *HA*- *receptor* in lymphocytes. This observation was substantiated by anti-34 kDa HA-binding protein antibodies immunoblotting and 125I-HA ligand blotting of lymphocytes cell lysate. The HA-induced cell aggregation, tyrosine phosphorylation and cytoskeletal protein phosphorylation demonstrate the HA-induced early cellular signalling events in lymphocytes. Further, to study the involvement of 34 kDa HA-binding protein in mitogen induced lymphocyte signalling, we studied in vivo phosphorylation and secondary messenger formation. The enhanced 34 kDa HA-binding protein phosphorylation by HA and the inhibition of cellular aggregation and IP3 formation by anti-HA-binding protein antibodies revealed that 34 kDa HA-binding protein is one of the potential mediators in HA-induced signal transduction.

7/3,AB/48 (Item 48 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

09102272 97021287 PMID: 8867647
Histochemical studies of *hyaluronan* and the *hyaluronan* *receptor* ICAM-1 in psoriasis.
Gustafson S; Wikstrom T; Juhlin L
Department of Medical & Physiological Chemistry, University of Uppsala, Sweden.
International journal of tissue reactions (SWITZERLAND) 1995, 17 (4) p167-73, ISSN 0250-0868 Journal Code: 8302116
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
Histochemical stainings of frozen sections of human normal and psoriatic skin were used to study the localization of hyaluronan (HA) and intercellular adhesion molecule 1 (ICAM-1). HA staining was found in all areas of the skin, with the exception of the stratum corneum, in both normal and psoriatic cases without any apparent quantitative differences between the conditions. The staining for ICAM-1 was detected in vessels in normal skin and at lower levels in normal areas of the skin in patients with psoriasis. However, in these patients the staining increased to about the same level as in normal skin after hyaluronidase treatment of the sections prior to staining. In psoriatic lesions, distinct staining for ICAM-1 was localized mainly to vessels and infiltrating leukocytes. Treatment of the sections with hyaluronidase increased the staining of vessels only slightly, but more strongly around leukocytes. These findings show that ICAM-1 is predominantly free from bound HA on vessel endothelium in psoriasis lesions but not on vessels in normal areas of the skin, and suggests that systematically administered HA, previously shown to reduce chronic inflammation in animal models, might have a beneficial effect in psoriasis via blocking of endothelial ICAM-1 and thereby causing a reduced invasion of leukocytes into the skin.

7/3,AB/49 (Item 49 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

09102269 97021284 PMID: 8867644
The role of *hyaluronan* and its receptors in restenosis after balloon angioplasty: development of a potential therapy.
Savani R C; Turley E A
Department of Pediatrics, University of Manitoba, Winnipeg, Canada. International journal of tissue reactions (SWITZERLAND) 1995, 17 (4) p141-51, ISSN 0250-0868 Journal Code: 8302116
Document type: Journal Article; Review; Review, Tutorial
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
Atherosclerosis is a progressive condition that is initiated by endothelial injury, promoted by growth factors, and which results in the formation of fibrofatty plaques that narrow the affected blood vessel. Balloon angioplasty is used to dilate these plaques in the coronary circulation so as to prevent

occlusion of this critical blood supply. However, 30-50% of balloon dilatations end in restenosis within six months of the procedure. The pathogenesis of both atherosclerosis and restenosis after balloon angioplasty involves the migration of medial smooth-muscle cells across the internal elastic lamina to form a neointima. Proliferation of these cells and their elaboration of an extracellular matrix results in stenosis of the affected area. Investigation of several animal models, as well as of the human condition, indicates the presence of an ongoing inflammatory reaction involving T cells and other leukocytes which probably maintain smooth-muscle cell migration, proliferation and matrix deposition. We have shown that the stenotic response involves the expression of HA (hyaluronan) receptors on both the infiltrating white cells and on smooth-muscle cell populations. Thus, in vitro, the locomotion and chemotaxis of these cells in response to injury is inhibited by reagents that block *HA*-*receptor* interactions including HA-binding peptides and high doses of HA. Further, the expression of these HA receptors is up-regulated after balloon-catheter injury of the rat carotid artery, and exposure of injured arteries to high concentrations of HA in vivo results in significant inhibition of neointimal formation. The possible clinical benefits of this response are discussed.

7/3,AB/50 (Item 50 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

09026400 96399609 PMID: 8806080
HA receptors: regulators of signalling to the cytoskeleton. Entwistle J; Hall C L; Turley E A
Manitoba Institute of Cell Biology, University of Manitoba, Winnipeg, Canada.
Journal of cellular biochemistry (UNITED STATES) Jun 15 1996, 61 (4) p569-77, ISSN 0730-2312 Journal Code: 8205768
Document type: Journal Article; Review; Review, Tutorial
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
Hyaluronan (HA) is a ubiquitous component of the extracellular matrix (ECM) and occurs transiently in both the cell nucleus and cytoplasm. It has been shown to promote cell motility, adhesion, and proliferation and thus it has an important role in such processes as morphogenesis, wound repair, inflammation, and metastasis. These processes require massive cell movement and tissue reorganization and are always accompanied by elevated levels of HA. Many of the effects of HA are mediated through cell surface receptors, three of which have been molecularly characterized, namely CD44, RHAMM, and ICAM-1. Binding of the HA ligand to its receptors triggers signal transduction events which, in concert with other ECM and cytoskeletal components, can direct cell trafficking during physiological and pathological events. The HA mediated signals are transmitted, at least in part, by the activation of protein phosphorylation cascades, cytokine release, and the stimulation of cell cycle proteins. A variety of extracellular signals regulate the expression of both HA and the receptors necessitating that *HA*-*receptor* signalling is a tightly controlled process. Regulated production of soluble forms of the receptors, alternately spliced cell surface isoforms, and glycosylation variants of these receptors can dramatically modulate HA binding, ligand specificity, and stimulation of the signalling pathway. When these processes are deregulated cell behaviour becomes uncontrolled leading to developmental abnormalities, abnormal physiological responses, and tumorigenesis. The elucidation of the molecular mechanisms regulating HA-mediated events will not only contribute greatly to our understanding of a variety of disease processes but will also offer many new avenues of therapeutic intervention.

7/3,AB/51 (Item 51 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

09026218 96394510 PMID: 8798616
The cell adhesion molecule, GP116, is a new CD44 variant (ex14/v10) involved in *hyaluronic* acid binding and endothelial cell proliferation.
Lokeshwar V B; Iida N; Bourguignon L Y
Department of Cell Biology and Anatomy, University of Miami School of Medicine, Miami, Florida 33101, USA.
Journal of biological chemistry (UNITED STATES) Sep 27 1996, 271 (39) p23853-64, ISSN 0021-9258 Journal Code: 2985121R
Contract/Grant No.: 1F32CA06047; CA; NCI; CA 66163; CA; NCI; GM 36353; GM ; NIGMS
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
In this study we have found that endothelial cells from different origins all contain a CD44-related transmembrane glycoprotein, named GP116. Using a bovine aortic endothelial cell line and a standard pulse-chase protocol, we show that GP116 is synthesized as a 52-kDa nascent polypeptide precursor (p52) which is processed to GP116 as follows, p52 --> p63/65 --> p82 --> p100 --> GP116. GP116 contains approximately 8 N- and approximately 11 O-linked oligosaccharide chains (but lacks glycosaminoglycans) and interacts directly with the cytoskeletal protein, ankyrin, both in vitro (Kd approximately 1.2 nM) and in vivo. The results of GP116 amino acid composition, reverse transcriptase-polymerase chain reaction, Southern blot, Northern blot, cloning, and sequence analyses

indicate that endothelial cells express this new CD44 variant that contains an exon having significant homology with human CD44 exon 14 (ex14/v10). GP116, designated as CD44 (ex14/v10), has been shown to be a major hyaluronic acid (*HA*) *receptor* (Kd approximately 0.5-0.8 nM) responsible for cell adhesion. Most importantly, we have found that the interaction between CD44(ex14/v10) and HA or a small fragment of HA (10-15 disaccharide units) induces a mitogenic response in endothelial cells. These findings suggest that this CD44 variant plays an important role in regulating endothelial cell proliferation.

7/3,AB/52 (Item 52 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

09026146 96394438 PMID: 8798544
Functional cloning of the cDNA for a human *hyaluronan* synthase. Shyjan A M; Heldin P; Butcher E C; Yoshino T; Briskin M J LeukoSite Inc., Cambridge, Massachusetts 02142, USA.
Journal of biological chemistry (UNITED STATES) Sep 20 1996, 271 (38) p23395-9, ISSN 0021-9258 Journal Code: 2985121R
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
Hyaluronan is a constituent of the extracellular matrix of connective tissue and is actively synthesized during wound healing and tissue repair to provide a framework for ingrowth of blood vessels and fibroblasts. Changes in the serum concentration of hyaluronan are associated with inflammatory and degenerative arthropathies such as rheumatoid arthritis. In addition, hyaluronan has been implicated as an important substrate for migration of adhesion of leukocytes during inflammation. A human hyaluronan synthase (HuHAS1) cDNA was isolated by a functional expression cloning approach. Transfection of CHO cells conferred hyaluronidase-sensitive adhesiveness of a mucosal T cell line via the lymphocyte *hyaluronan* *receptor* , CD44, as well as increased hyaluronan levels in the cultures of transfected cells. The HuHAS1 amino acid sequence shows considerable homology to the hasA gene product of Streptococcus pyogenes, a glycosaminoglycan synthetase from Xenopus laevis (DG42), and is the human homolog of a recently described murine hyaluronan synthase.

7/3,AB/53 (Item 53 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

08995072 96350253 PMID: 8764866
Spatial distribution of CD44 and *hyaluronan* in the proximal tibia of the growing rat.
Noonan K J; Stevens J W; Tammi R; Tammi M; Hernandez J A; Midura R J Department of Orthopaedic Surgery, University of Iowa, College of Medicine, Iowa City 52242, USA.
Journal of orthopaedic research : official publication of the Orthopaedic Research Society (UNITED STATES) Jul 1996, 14 (4) p573-81, ISSN 0736-0266 Journal Code: 8404726
Contract/Grant No.: AR-070S; AR; NIAMS
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
CD44 has been described as a cell surface *hyaluronan* *receptor* present on a variety of different cells, and it is generally assumed to be prevalent in most connective tissues that contain hyaluronan. A major aim of this study was to test that presumption by localizing CD44 and hyaluronan within several tissues of the proximal tibia of the growing rat. Comparison of these profiles would reveal whether CD44 and hyaluronan co-localize with high fidelity, as would be expected if CD44 were a major hyaluronan binding protein. Using in situ hybridization and immunohistochemistry, CD44 was identified on osteoclasts, chondroclasts, osteocytes, hematopoietic marrow cells, synovial cells, and connective tissue fibroblasts (ligaments, tendons, and fascia). Although the majority of osteocytes expressed CD44, reduced expression was observed for osteoblasts and ostcoprogenitor cells. Additionally. CD44 was not detected on chondrocytes from epiphyseal and metaphyseal growth cartilages or in meniscal fibrocartilage. Using biotinylated G1 domain from aggrecan and link protein, hyaluronan was observed in the maturational and hypertrophic zones of all growth cartilages, the synovium and other fibroblastic connective tissues, regional areas of the periosteum and endosteum (around osteoblasts, osteoprogenitor cells, and osteoclasts), osteocyte lacunae, and surrounding blood vessels. In regions of co-localization for CD44 and hyaluronan, it seems that CD44 is a likely hyaluronan binding protein in several tissues of the proximal tibia. However, it does not appear to be the predominant hyaluronan binding protein in growing cartilages of the weanling rat.

7/3,AB/54 (Item 54 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

08969386 96320805 PMID: 8739496
Hyaluronan, CD44 and fibronectin in rabbit corneal epithelial wound healing.
Asari A; Morita M; Sekiguchi T; Okamura K; Horie K; Miyauchi S Tokyo Research Institute, Seikagaku

Corporation, Japan.
Japanese journal of ophthalmology (JAPAN) 1996, 40 (1) p18-25, ISSN 0021-5155 Journal Code: 0044652
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
Changes in hyaluronan (HA) concentration and stainability were investigated in the rabbit cornea after wounds made by exposure to n-heptanol. The HA concentration in the cornea increased gradually until day 14 after wounding, and then decreased. The HA concentration returned to the normal level 56 days after wounding. In the normal control cornea, HA staining was observed in the epithelium and stroma. The intensity of HA staining in the epithelium and stroma increased until day 3 after wounding, when the epithelium had completely covered the defect. At day 28, when the thickness of the corneal epithelium returned to the normal level, the intensity of HA staining in the epithelium also decreased. However, staining in the stroma was still strong. HA staining in the stroma decreased by day 56 after wounding. In parallel experiments, the immunostaining for CD44, an *HA* *receptor*, and fibronectin (FN) was carried out in the same model. The immunostaining in the epithelium of both CD44 and FN was synchronistic with the HA staining during the early stages after wounding. These events suggest that HA, CD44 and FN cooperatively play important roles in corneal epithelial wound healing.

7/3,AB/55 (Item 55 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

08926405 96279031 PMID: 8663000
Transforming growth factor-beta1 stimulates multiple protein interactions at a unique cis-element in the 3'-untranslated region of the *hyaluronan* *receptor* RHAMM mRNA.
Amara F M; Entwistle J; Kuschak T I; Turley E A; Wright J A Manitoba Institute of Cell Biology, University of Manitoba, Winnipeg, Manitoba R3E 0V9, Canada.
Journal of biological chemistry (UNITED STATES) Jun 21 1996, 271 (25) p15279-84, ISSN 0021-9258 Journal Code: 2985121R
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
The receptor for hyaluronan mediated motility (RHAMM) gene expression is markedly elevated in fibrosarcomas exposed to transforming growth factor-beta1 (TGF-beta1). The half-life of RHAMM mRNA was increased by 3 fold in cells treated with TGF-beta1, indicating that growth factor regulation of RHAMM gene expression at least in part involves a posttranscriptional mechanism. Our studies demonstrated that a unique 30-nucleotide (nt) region that has three copies of the sequence, GCUUGC, was the TGF-beta1-responsive region in the 3'-untranslated region (3'-UTR) that mediated message stability. This region interacted specifically with cytoplasmic trans-factors to form multiple protein complexes of approximately 175, 97, 63, 26, and 17 kDa post-TGF-beta1 treatment, suggesting a role for these complexes in the mechanism of action of TGF-beta1-induced message stabilization. Insertion of the 3'-UTR into the chloramphenicol acetyltransferase gene conferred TGF-beta1 induced stability of chloramphenicol acetyltransferase-hybrid RNA in stably transfected cells, while the same insert carrying a deletion containing the 30-nt region had no significant effect on mRNA stability. These results provide a model of RHAMM message regulation in which TGF-beta1-mediated alteration of RHAMM message stability involves the up-regulation of multiple protein interactions with a 30-nt cis-element stability determinant in the 3'-UTR. This model also suggests that this 30-nt base region functions in cis to destabilize RHAMM mRNA in resting normal cells.

7/3,AB/56 (Item 56 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

08904356 96266972 PMID: 8674281
Epidermal growth factor modulates cell attachment to *hyaluronic* acid by the cell surface glycoprotein CD44.
Zhang M; Singh R K; Wang M H; Wells A; Siegal G P
Department of Pathology, University of Alabama at Birmingham, USA. Clinical & experimental metastasis (ENGLAND) May 1996, 14 (3) p268-76, ISSN 0262-0898 Journal Code: 8409970
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
Cell adhesion to and migration through extracellular matrices (ECM) are critical events in tumor invasion and metastasis. Previous work by us had demonstrated that signaling of epidermal growth factor receptor (EGFR) confers an oncogenic phenotype on NR6 cells and that these cells when transfected with holo EGFR demonstrate greater motility and invasiveness than cells carrying a carboxy-terminal truncated EGFR. Recently, a cell surface glycoprotein, CD44, has been implicated in cell-ECM adhesion involved in tumor cell migration, signal transduction, and metastasis. We investigated whether EGF regulates cellular interactions with ECM components, and in particular, hyaluronate, by modulating CD44 expression. In vitro cell attachment assays on hyaluronate-coated plates demonstrated similar

basal level of binding (approximately 33%) for murine NR6 parental cells devoid of endogenous EGFR (P) or expressing wild-type EGFR (WT), while a time-dependent increase in binding was observed in WT cells stimulated with EGF. Additionally, utilizing monoclonal antibody blocking assays, CD44, but not EGFR, was shown to be directly involved in this attachment. Both WT and P cells possessed equivalent 95 kDa bands on immunoblots, corresponding to CD44. The existence of CD44 mRNA was verified by RT-PCR using synthetic oligonucleotides in which a 1.1 kb cDNA was detected in both cell lines and confirmed by DNA sequencing. After 24-h exposure to exogenous EGF, an increase in CD44 protein and mRNA expression was found in WT cells, but not in P cells, supporting the contention that a functional EGFR signaling pathway is required for CD44 regulation. Thus, EGF stimulates cell binding to hyaluronate in vitro by regulating CD44 expression.

7/3,AB/57 (Item 57 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

08901938 96261667 PMID: 8666924
Soluble *hyaluronan* *receptor* RHAMM induces mitotic arrest by suppressing Cdc2 and cyclin B1 expression.
Mohapatra S; Yang X; Wright J A; Turley E A; Greenberg A H Manitoba Institute of Cell Biology, University of Manitoba, Winnipeg, Canada.
Journal of experimental medicine (UNITED STATES) Apr 1 1996, 183 (4) p1663-8, ISSN 0022-1007 Journal Code: 2985109R
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
The hyaluronan (*HA*) *receptor* RHAMM is an important regulator of cell growth. Overexpression of RHAMM is transforming and is required for H-ras transformation. The molecular mechanism underlying growth control by RHAMM and other extracellular matrix receptors remains largely unknown. We report that soluble RHAMM induces G2/M arrest by suppressing the expression of Cdc2/Cyclin B1, a protein kinase complex essential for mitosis. Down-regulation of RHAMM by use of dominant negative mutants or antisense of mRNA also decreases Cdc2 protein levels. Suppression of Cdc2 occurs as a result of an increased rate of cdc2 mRNA degradation. Moreover, tumor cells treated with soluble RHAMM are unable to form lung metastases. Thus, we show that mitosis is directly linked to RHAMM through control of Cdc2 and Cyclin B1 expression. Failure to sustain levels of Cdc2 and Cyclin B1 proteins leads to cell cycle arrest.

7/3,AB/58 (Item 58 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

08884444 96243191 PMID: 8675189
Biosynthesis and degradation of *hyaluronan* by nonparenchymal liver cells during liver regeneration.
Vrochides D; Papanikolaou V; Pertoft H; Antoniades A A; Heldin P Department of Medical and Physiological Chemistry, Biomedical Center, Uppsala University, Sweden.
Hepatology (Baltimore, Md.) (UNITED STATES) Jun 1996, 23 (6) p1650-5 , ISSN 0270-9139 Journal Code: 8302946
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
Hepatic stellate cells (HSC) and endothelial cells of the liver sinusoids synthesize and degrade hyaluronan, respectively. The roles of these cell types in the biosynthesis and degradation of hyaluronan were studied during regeneration following partial hepatectomy. Pure cultures of HSC and liver endothelial cells (LEC) were obtained from regenerating liver at different stages using a Nycodenz gradient followed by discontinuous Percoll gradient. The HSC that established 3 or 4 days after partial hepatectomy synthesized large amounts of hyaluronan when cultured in the presence of fetal calf serum (FCS) or platelet-derived growth factor B-chain homodimer (PDGF)-BB. These cells, as well as LEC, expressed active PDGF beta-receptors. Furthermore, the ability of LEC to degrade hyaluronan was decreased at early stages of liver regeneration. The increased synthesis of hyaluronan by HSC and the failure of LEC to catabolize the polysaccharide resulted in elevated hyaluronan concentrations in the blood.

7/3,AB/59 (Item 59 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

08883396 96234257 PMID: 8669459
Increased *hyaluronan* at sites of attachment to mesentery by CD44-positive mouse ovarian and breast tumor cells.
Yeo T K; Nagy J A; Yeo K T; Dvorak H F; Toole B P Department of Anatomy and Cellular Biology, Tufts University School of Medicine, Boston, MA 02111, USA.
American journal of pathology (UNITED STATES) Jun 1996, 148 (6) p1733-40, ISSN 0002-9440 Journal Code: 0370502
Contract/Grant No.: CA58845; CA; NCI; DE05838; DE; NIDCR; HD23681; HD; NICHD
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed

The mouse ovarian ascites tumor, MOT, and mammary ascites tumor, TA3/St, served as models to follow changes in hyaluronan levels during tumor growth, attachment, and invasion. Subsequent to introduction of tumor cells into the peritoneal cavity, hyaluronan accumulated intraperitoneally and at the initial sites of attachment of tumor cells and cell clumps to the mesenteric surface; the latter co-localized with sites of fibrin deposition as reported earlier. Subsequently, high levels of hyaluronan accumulated throughout the interior of the mesentery. Because neither tumor cell line synthesized substantial amounts of hyaluronan in culture, the large accumulations observed in the mesenteries and ascites fluid of tumor-bearing animals most likely resulted from increased synthesis and secretion by peritoneal-lining mesothelial cells and/or fibroblasts in response to stimulation by the tumor cells or their products. TA3/St tumor cells were universally positive for the *hyaluronan* *receptor*, CD44, whereas approximately 90% of MOT tumor cells were CD44-negative. However, the great majority of MOT or TA3/St cells that initially attached to the mesentery were strongly CD44 positive. We propose that hyaluronan-rich matrix is involved in tumor cell attachment to the mesentery possibly via interaction with tumor cell surface CD44.

7/3,AB/60 (Item 60 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

08878616 96239590 PMID: 8649770
Overexpression of CD44 in pl85(neu)-transfected NIH3T3 cells promotes an up-regulation of *hyaluronic* acid-mediated membrane-cytoskeleton interaction and cell adhesion.
Zhu D; Bourguignon L
Department of Cell Biology and Anatomy, School of Medicine, University of Miami, Florida 33101, USA.
Oncogene (ENGLAND) Jun 6 1996, 12 (11) p2309-14, ISSN 0950-9232 Journal Code: 8711562
Contract/Grant No.: CA66163; CA; NCI; GM36353; GM; NIGMS Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
CD44 is a transmembrane glycoprotein known to bind hyaluronic acid (HA) in its extracellular domain and to contain at least one ankyrin-binding site in its cytoplasmic domain. In this study we have examined CD44 expression in a mouse fibroblast cell line transfected with the pl85(neu) oncogene cDNA. The results of RT-PCR and Southern blot analyses reveal that CD44s (CD44 standard form) transcript is expressed in both pl85(neu)-transfected cells and untransfected cells. Using surface iodination, anti-CD44 immunoprecipitation and immuno-binding assays, we have found that the number of CD44s molecules expressed on the surface of pl85(neu)-transfected cells are at least 4.5-fold higher than those detected on untransfected cells. Overexpression of surface CD44s in pl85(neu)-transfected cells results in a dramatic enhancement of HA-mediated cell adhesion. Scatchard plot analysis indicates that CD44s in pl85(neu) transfected cells binds directly and specifically to ankyrin. The binding affinity between CD44s and ankyrin in p185(neu)-transfected cells approximately 0.19 nM) appears to be somewhat higher than that found in the untransfected cells (K(p) approximately 0.30 nM). Double immunofluorescence staining and confocal microscopic analyses indicate that HA induces the *HA* *receptor* (i.e. CD44s) to form adhesion plaque-like structures, and causes an accumulation of intracellular ankyrin directly underneath *HA* *receptor* (CD44s)-adhesion plaque-like structures in pl85(neu)-transfected cells (but not in untransfected cells). These findings suggest that overexpression of CD44s and up-regulation of CD44s-ankyrin interaction by pl85(neu) oncogene may be one of the pre-requisite steps in regulating tumor cell behavior.

7/3,AB/61 (Item 61 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

08864256 96227139 PMID: 8654848
Modulation of the *hyaluronan* *receptor* , CD44, by its transmembrane and cytoplasmic domains.
Sheikh H; Uff C R; Peck D; Isacke C M
Department of Biology, Imperial College of Science, Technology and Medicine, London, U.K.
Biochemical Society transactions (ENGLAND) Nov 1995, 23 (4) p831-5, ISSN 0300-5127 Journal Code: 7506897
Document type: Journal Article; Review; Review, Tutorial
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed

7/3,AB/62 (Item 62 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

08771711 96121957 PMID: 7496149
Accessible *hyaluronan* receptors identical to ICAM-1 in mouse mast-cell tumours.
Gustafson S; Bjorkman T; Forsberg N; Lind T; Wikstrom T; Lidholt K Department of Medical and Physiological Chemistry, University of Uppsala, Sweden.
Glycoconjugate journal (ENGLAND) Jun 1995, 12 (3) p350-5, ISSN 0282-0080 Journal Code: 8603310
Document type: Journal Article

Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
Immunohistochemical studies of the hyaluronan (*HA*)-*receptor* (R), originally found on liver endothelial cells (LEC) and related to the intercellular adhesion molecule 1 (ICAM-1), showed that polyclonal antibodies against HARLEC (*HA* *receptor* on LEC) also stain structures in mouse mastocytomas, mainly vessels. To test if intravenously administered HA might target the tumour receptors in vivo, mice carrying an inoculated mastocytoma in one hind leg muscle were injected in the tail vein with 125I-tyrosine (T)-labelled HA and killed 75 min after injection when organs and tissues were checked for radioactivity. When doses exceeding the binding capacity of the liver were injected, a significant increase in radioactivity (up to five-fold) within the tumour tissue was found. The weight adjusted difference between control and tumour tissue was greater for smaller tumours, probably due to necrosis in the larger. HA-staining of tumours from animals receiving 125I-T-HA, showed HA in areas that also stained weakly for ICAM-1 using monoclonal antibodies. ICAM-1 staining was dramatically increased after hyaluronidase treatment of the sections, indicating that the HA is bound to these receptors and thereby blocks antibody recognition.

7/3,AB/63 (Item 63 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

08767427 96114079 PMID: 8846023
Induction of a *hyaluronan* *receptor*, CD44, during embryonal carcinoma and embryonic stem cell differentiation.
Wheatley S C; Isacke C M
Department of Biology, Imperial College for Science, Technology and Medicine, London, England.
Cell adhesion and communication (SWITZERLAND) Aug 1995, 3 (3) p217-30, ISSN 1061-5385 Journal Code: 9417027
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
This paper describes the expression profile of the CD44 glycoprotein during differentiation of embryonal carcinoma (EC) and embryonic stem (ES) cells. We have recently shown that CD44 is expressed in discrete embryonic structures and, in view of this, we sought an in vitro differentiation model of development in which we could study more readily the structure and function of the CD44 molecule. The P19 EC and CGR8 ES cells were chosen as they have the capacity to develop down the cardiac muscle pathway and we have previously demonstrated that CD44 is expressed abundantly in the embryonic myocardium. The differentiation process in both cell types is accompanied by an induction of CD44 mRNA and protein. However, in differentiated cultures CD44 is not expressed in contractile cells, indicating that these P19 cells do not represent CD44-positive embryonic cardiomyocytes. Expression of CD44 is observed on fibroblast-like cells which appear to migrate over and out from the plated aggregates. Hyaluronan, the major ligand for CD44, is also associated with these CD44-positive fibroblast-like cells. It is suggested that expression of both receptor and ligand by the fibroblast cells is required for cell:matrix adhesion and cell motility. As CD44 is up-regulated in these cultures, P19 cells are now established as a useful model system to study the factors regulating expression of the CD44 gene.

7/3,AB/64 (Item 64 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

08724101 96078141 PMID: 7480006
Hyaluronan *receptor* antagonists alter skin inflammation and fibrosis following injury.
Savani R C; Khalil N; Turley E A
Department of Pediatrics, Manitoba Institute of Cell Biology, University of Manitoba, Winnipeg, Canada.
Proceedings of the Western Pharmacology Society (UNITED STATES) 1995, 38 p131-6, ISSN 0083-8969 Journal Code: 7505899
Document type: Journal Article; Review; Review, Tutorial
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed

7/3,AB/65 (Item 65 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

08720919 96070535 PMID: 7472951
Hyaluronic acid metabolism in keloid fibroblasts.
Alaish S M; Yager D R; Diegelmann R F; Cohen I K
Wound Healing Center, Medical College of Virginia/Virgina Commonwealth University, Richmond 23298-0117, USA.
Journal of pediatric surgery (UNITED STATES) Jul 1995, 30 (7) p949-52, ISSN 0022-3468 Journal Code: 0052631
Contract/Grant No.: GM-20298; GM; NIGMS
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
Hyaluronic acid (HA), an important component of the tissue extracellular matrix, is a ubiquitous

glycosaminoglycan (GAG) that forms a pericellular coat on the surface of cells. It has been speculated that this pericellular HA boundary may localize cytokines, such as transforming growth factor-beta 1, which is known to stimulate collagen production. The purpose of this study was to examine the role of HA and its cell surface receptor (CD44), an active participant in HA degradation, as they relate to keloid formation. Dermal excisions from both normal patients (n = 13) and keloid patients (n = 13) were analyzed for HA content using an alcian blue staining technique. Fibroblast cell cultures were used to quantitate HA synthesis and CD44 receptor density. Histological analyses showed a greater HA content in keloid tissue compared with normal dermal tissue. In agreement with this observation, keloid fibroblasts were found to synthesize significantly more HA than normal dermal fibroblasts (2469 +/- 483 cpm versus 1122 +/- 256 cpm, P = .02). Treatment of keloid fibroblasts with triamcinolone acetonide reduced the level of HA synthesis to that of normal fibroblasts (1560 +/- 477 cpm versus 1293 +/- 264 cpm, P = .6). However, there was no significant difference in *HA* *receptor* density on keloid cells compared with normal skin fibroblasts. Therefore, the increased HA deposits found in keloids are attributable to increased synthesis rather than to decreased degradation mediated by the CD44 receptor.

7/3,AB/66 (Item 66 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

08718326 96071026 PMID: 7591247
Hyaluronic acid/CD44H interaction induces cell detachment and stimulates migration and invasion of human glioma cells in vitro. Koochekpour S; Pilkington G J; Merzak A
Department of Neuropathology, Institute of Psychiatry, London, UK. International journal of cancer. Journal international du cancer (UNITED STATES) Nov 3 1995, 63 (3) p450-4, ISSN 0020-7136 Journal Code: 0042124
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
The mechanisms underlying the invasive properties of gliomas, the major form of intrinsic brain tumours in humans, are poorly understood. We have reported that CD44 plays an important role in this behaviour in vitro. In the present work, we investigated the role of its ligand, hyaluronic acid (HA), in invasion in 8 human glioma cell lines. We found that HA mediates cell detachment via its interaction with its high affinity receptor, CD44H. Using 8 microns porosity polycarbonate filter transwells, we demonstrate that HA strongly stimulates migration in all 8 cell lines. This effect was found to be partially counteracted by a CD44H monoclonal antibody (MAb), suggesting the involvement of CD44H, as well as other HA receptors, in this process. Furthermore, incorporation of increasing concentrations of HA in Matrigel in an in vitro invasion assay resulted in a substantial increase in the invasive propensity of the glioma cell lines. Moreover, blocking experiments with the CD44H MAb suggest that CD44H and other receptors interact with HA to promote cell invasion in vitro. Our results show that HA induces cell detachment, stimulates migration and promotes invasion via its interaction with CD44H and other HA receptors in vitro. These effects could be prevented by use of specific *HA* *receptor* antibodies.

7/3,AB/67 (Item 67 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

08671762 96011639 PMID: 7590272
Characterization of the murine gene encoding the *hyaluronan* *receptor* RHAMM.
Entwistle J; Zhang S; Yang B; Wong C; Li Q; Hall C L; A J; Mowat M; Greenberg A H; Turley E A
Manitoba Institute of Cell Biology, Manitoba Cancer Treatment and Research Foundation, Winnipeg, Canada.
Gene (NETHERLANDS) Oct 3 1995, 163 (2) p233-8, ISSN 0378-1119 Journal Code: 7706761
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
We describe the isolation and characterization of the murine gene encoding RHAMM, a *hyaluronan* *receptor* which regulates focal adhesion turnover, is required for cell locomotion and is a critical downstream regulator of ras transformation. The RHAMM gene spans at least 20 kb and comprises 14 exons ranging in size from 75 to 1099 bp. Primer extension studies indicate that the major transcription start point is in position -31, relative to the start Met. Northern blot analysis of mouse fibroblast RNA identified two hybridizing species of 4.2 and 1.7 kb. Comparison of cDNA clones and RT-PCR products with the genomic clones identified alternately spliced exons in both the coding and 5' noncoding regions of RHAMM. In the coding region exon 4 is alternately spliced. The major RHAMM transcript (RHAMM1) in 3T3 fibroblasts does not contain exon 4 and encodes a protein of 70 kDa. A minor transcript containing exon 4, namely RHAMM v4, encodes a 73-kDa protein, as demonstrated by isoform-specific antibodies. Western analysis demonstrated both a major 70-kDa (RHAMM 1) and minor 73-kDa RHAMM protein (v4) in 3T3 murine fibroblast cell lysates. The functional significance of these two isoforms is currently being investigated.

7/3,AB/68 (Item 68 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

08620851 95378321 PMID: 7544357
Interaction of CD44 variant isoforms with *hyaluronic* acid and the cytoskeleton in human prostate cancer cells.
Welsh C F; Zhu D; Bourguignon L Y
Department of Cell Biology and Anatomy, University of Miami Medical School, Florida 33101, USA.
Journal of cellular physiology (UNITED STATES) Sep 1995, 164 (3) p605-12, ISSN 0021-9541 Journal Code: 0050222
Contract/Grant No.: CA66163; CA; NCI; GM36353; GM; NIGMS Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
CD44 is a glycosylated adhesion molecule which may undergo alternative splicing of 10 possible exons to generate variant isoforms. A number of CD44 variant isoforms expressed by tumor cells have been correlated with metastatic and proliferative behavior. In this study, we have characterized CD44 isoform expression on three prostate cancer cell lines: ALVA-31, PPC-1, and LNCaP. Using reverse transcriptase-polymerase chain reaction, we have found that ALVA-31 and PPC-1 cells express multiple CD44 isoforms, including CD44s (standard form), CD44E (epithelial form), and an exon 14-containing form. In addition, two smaller forms have been detected: one using an alternative donor splice site within exon 5, and a novel form omitting exon 5 entirely. The CD44 isoforms expressed by ALVA-31 and PPC-1 cells appear to be preferentially located on the cell surface. By contrast, LNCaP cells do not express any of the CD44 forms at the RNA or protein level. Both PPC-1 and ALVA-31 cells display tumorigenesis and invasiveness in nude mice, whereas LNCap cells exhibit a less malignant phenotype, suggesting a correlation between CD44 variant (CD44v) expression and aggressive prostate tumor behavior. Functional characterization reveals that CD44 mediates prostate cell adhesion to extracellular hyaluronic acid (HA). In addition, the CD44 cytoplasmic domain binds specifically to ankyrin, a membrane cytoskeletal protein. Double immunofluorescence labeling and confocal microscopic analyses indicate that HA binding induces the *HA* *receptor* (i.e., CD44) to form capped structures. Importantly, intracellular ankyrin is preferentially accumulated underneath *HA* *receptor* -capped structures. These results suggest that cytoskeletal proteins such as ankyrin are closely associated with CD44-mediated signaling events induced by HA. Finally, HA-mediated transmembrane interactions between CD44 isoforms and cytoskeletal proteins (i.e. ankyrin) may play a pivotal role in regulating tumor cell behavior during human prostate cancer development.

7/3,AB/69 (Item 69 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

08608682 95368652 PMID: 7543820
Functional *hyaluronan* receptors are expressed on a squamous cell lung carcinoma cell line but not on other lung carcinoma cell lines. Teder P; Bergh J; Heldin P
Department of Medical and Physiological Chemistry, Uppsala University, Sweden.
Cancer research (UNITED STATES) Sep 1 1995, 55 (17) p3908-14, ISSN 0008-5472 Journal Code: 2984705R
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
We investigated the production of hyaluronan and the presence of hyaluronan receptors in a panel of human lung carcinoma cell lines, consisting of small cell carcinomas (SCLC) and non-small cell carcinomas (non-SCLC). These transformed cell lines produced only minute amounts of hyaluronan, whereas normal lung fibroblasts synthesized high amounts. CD44 molecules (an integral membrane glycoprotein suggested previously to function as a *hyaluronan* *receptor*) were differentially expressed on non-SCLC cell lines but essentially not on the SCLC cell lines. In contrast, RHAMM molecules (receptor for hyaluronan-mediated motility) were preferentially expressed on SCLC cells. Although all the lung tumor cell lines expressed various amounts of CD44 and RHAMM, only the SCLC line U-1752 could bind [3H]hyaluronan. The binding sites were saturated with about 19,700 hyaluronan molecules (Mr 1.4 x 10(6)) bound per cell with a Kd of 0.16 x 10(-9) M. CD44 molecules were responsible for the binding activity since Hermes-1 antibodies that block the binding of hyaluronan to CD44 blocked the binding of [3H]hyaluronan to U-1752 cells. 4-Phorbol 12-myristate 13-acetate (PMA) treatment of U-1752 cells both increased the hyaluronan-binding activity in U-1752 cells as well as induced abrogation of cell-cell and cell-matrix interactions. Addition of hyaluronan inhibited the PMA-induced disassembly of the cells. The fact that CD44 molecules are able to bind [3H]hyaluronan only on the SCLC line U-1752 but not on other lung carcinoma cell lines may be of value as a marker for squamous cell carcinoma differentiation. Furthermore, the inhibitory effect of hyaluronan on the PMA-promoted cell disassembly suggest that hyaluronan surrounding squamous cell carcinoma cells may affect their migration and invasiveness.

7/3,AB/70 (Item 70 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

08597424 95355842 PMID: 7543138
Variant cell lines selected for alterations in the function of the *hyaluronan* *receptor* CD44 show differences in glycosylation. Lesley J; English N; Perschl A; Gregoroff J; Hyman R
Department of Cancer Biology, The Salk Institute, San Diego, California 92186-5800, USA.
Journal of experimental medicine (UNITED STATES) Aug 1 1995, 182 (2) p431-7, ISSN 0022-1007 Journal Code: 2985109R
Contract/Grant No.: AI-31613; AI; NIAID; CA-14195; CA; NCI Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
CD44 is a major cell surface receptor for the extracellular matrix glycosaminoglycan hyaluronan (HA). However, the ability of CD44 to bind ligand is strictly regulated. Three activation states of CD44 have been demonstrated: (a) inactive; (b) inducible (by certain CD44-specific mAb); and (c) constitutively active. Starting with two parental cell lines expressing CD44 in the inactive state, a pre-B cell (RAW 253) and a fibroblast (L cells), we used fluorescence-activated cell sorting with fluorescein-conjugated hyaluronan in the presence of inducing mAb to derive variant cell lines with CD44 in the inducible state. Constitutively active derivatives were isolated from the inducible variants by a further round of fluorescence-activated cell sorting in the absence of inducing antibody. However, constitutively active variants could not be isolated directly from parental cells expressing CD44 in the inactive state. These results suggest that two genetic events must occur to obtain an active CD44-*HA* *receptor* from an inactive receptor. Variant and parental cell-derived CD44 molecules exhibited differences in migration on sodium dodecyl sulfate-polyacrylamide gel electrophoresis that were partly attributable to differences in N-linked glycosylation. Furthermore, culture in tunicamycin for 2-3 d converted parental and inducible cell lines into cells showing constitutive CD44-mediated HA binding. Also, removal of cell surface glycosaminoglycan chains by culture of cells in p-nitrophenyl beta-D-xylopyranoside or treatment with chondroitinase ABC resulted in conversion of cells with an inactive CD44 receptor to an inducible state. These results indicate that carbohydrate side chains of CD44 and/or other molecules on the cell surface that interact with CD44 are potentially involved in regulating the HA-binding function of CD44 on the cell surface.

7/3,AB/71 (Item 71 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

08589732 95347385 PMID: 7542594
Hyaluronan binding by CD44 is regulated by a phosphorylation-independent mechanism.
Uff C R; Neame S J; Isacke C M
Department of Biology, Imperial College of Science, Technology and Medicine, London, GB.
European journal of immunology (GERMANY) Jul 1995, 25 (7) p1883-7, ISSN 0014-2980 Journal Code: 1273201
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
CD44 is an adhesion receptor for which the major characterized ligand is the extracellular matrix glycosaminoglycan, hyaluronan. This interaction underlies CD44-mediated cell attachment, cell migration, and matrix remodelling during development and wound healing. Truncation of the CD44 cytoplasmic domain does not prevent cell surface expression of this *hyaluronan* *receptor* but it dramatically impairs ligand binding. In this study we have examined the role of phosphorylation in regulating this function by mutating the target serine residues to either neutral amino acids with the aim of creating a phosphorylation-incompetent molecule, or to acidic residues to mimic a fully phosphorylated CD44. In transfected AKR1 cells the behavior of both the neutral and acidic mutants was indistinguishable from wild-type CD44, indicating that there is a phosphorylation-independent mechanism involved in regulating hyaluronan binding.

7/3,AB/72 (Item 72 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

08571770 95330805 PMID: 7541721
Overexpression of the *hyaluronan* *receptor* RHAMM is transforming and is also required for H-ras transformation. Hall C L; Yang B; Yang X; Zhang S; Turley M; Samuel S; Lange L A; Wang C; Curpen G D; Savani R C; et al
Manitoba Institute of Cell Biology, University of Manitoba, Winnipeg, Canada.
Cell (UNITED STATES) Jul 14 1995, 82 (1) p19-26, ISSN 0092-8674 Journal Code: 0413066
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
Overexpression of the RHAMM gene by transfection into fibroblasts is transforming and causes spontaneous metastases in the lung. H-ras-transformed fibrosarcomas transfected with a dominant suppressor mutant of RHAMM exhibit a

so-called revertant phenotype and are completely nontumorigenic and nonmetastatic. Conversely, fibroblasts stably expressing low levels of RHAMM as a result of antisense transfection are resistant to ras transformation. Collectively, these results indicate that RHAMM acts downstream of ras. The loss of functional RHAMM ablates signaling within focal adhesions, in particular changes in focal adhesion kinase phosphorylation, and as a result these focal adhesions are unable to turn over in response to hyaluronan. These results provide evidence of the oncogenic potential of a novel extracellular matrix receptor and establish a functional link between transformation by ras and signaling within focal adhesions that are required for transformation by this oncogene.

7/3,AB/73 (Item 73 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

08475677 95230378 PMID: 7536236
Alternative RNA splicing of the *hyaluronic* *acid* *receptor* CD44 in the normal human brain and in brain tumors. Nagasaka S; Tanabe K K; Bruner J M; Saya H; Sawaya R E; Morrison R S Department of Neurosurgery, University of Texas M.D. Anderson Cancer Center, Houston, USA.
Journal of neurosurgery (UNITED STATES) May 1995, 82 (5) p858-63, ISSN 0022-3085 Journal Code: 0253357
Contract/Grant No.: NS26125; NS; NINDS; NS31775; NS; NINDS; PA-90-17; PHS ; +
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
The cell-surface receptor for hyaluronic acid, CD44, is expressed by both normal and malignant cells. Numerous CD44 isoforms have recently been identified that are derived by alternative ribonucleic acid splicing. The expression of some CD44 isoforms has been shown to be involved in tumor progression and metastatic spread in a rat carcinoma model and in human carcinomas. In the present study, CD44 isoform expression was evaluated by reverse transcriptase-polymerase chain reaction (PCR) analysis in frozen sections derived from three samples of normal brain tissue and from 40 brain tumors, including samples of glioblastoma multiforme, anaplastic astrocytoma, low-grade astrocytoma, cerebral primitive neuroectodermal tumor, medulloblastoma, metastatic colon carcinoma, and metastatic melanoma. Normal brain tissue adjacent to the tumors was also examined in 14 of 18 glioblastomas. In all normal brain and tumor samples, with the exception of metastases from colon carcinoma, PCR analysis demonstrated one prominent product that corresponded to the CD44H hematopoietic form of CD44. Metastases from colon carcinoma demonstrated two prominent PCR amplification products corresponding to CD44H and CD44R1. These results suggest that CD44H is the predominant isoform of this protein in normal human brain tissue and in human neuroectodermal tumors of varying degrees of malignancy. The ability of CD44H to mediate tumor cell motility and invasiveness (in contrast to CD44R1) suggests that the CD44 alternative splicing pattern of neuroectoderm-derived tumors may enhance their local biological aggressiveness and intracerebral spread. The lack of expression of larger molecular weight CD44 variants by primary brain tumors may also partially explain why these tumors rarely metastasize to distant sites.

7/3,AB/74 (Item 74 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

08445575 95190012 PMID: 7533785
Migration of bovine aortic smooth muscle cells after wounding injury. The role of *hyaluronan* and RHAMM. Savani R C; Wang C; Yang B; Zhang S; Kinsella M G; Wight T N; Stern R; Nance D M; Turley E A
Department of Pediatrics, University of Manitoba, Winnipeg, Canada. Journal of clinical investigation (UNITED STATES) Mar 1995, 95 (3) p1158-68, ISSN 0021-9738 Journal Code: 7802877
Contract/Grant No.: 18645; PHS
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
The migration of smooth muscle cells is a critical event in the pathogenesis of vascular diseases. We have investigated the role of hyaluronan (HA) and the *hyaluronan* *receptor* RHAMM in the migration of adult bovine aortic smooth muscle cells (BASMC). Cultured BASMC migrated from the leading edge of a single scratch wound with increased velocity between 1 and 24 h. Polyclonal anti-RHAMM antisera that block HA binding with this receptor abolished smooth muscle cell migration following injury. HA stimulated the random locomotion of BASMC and its association with the cell monolayer increased following wounding injury. Immunoblot analysis of wounded monolayers demonstrated a novel RHAMM protein isoform that appeared within one hour after injury. At the time of increased cell motility after wounding, FACS analysis demonstrated an increase in the membrane localization in approximately 25% of the cell population. Confocal microscopy of injured monolayers confirmed that membrane expression of this receptor was limited to cells at the wound edge. Collectively, these data demonstrate that RHAMM is necessary for the migration of smooth muscle cells and that expression and distribution of this receptor is tightly regulated following

wounding of BASMC monolayers.

7/3,AB/75 (Item 75 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

08435459 95197709 PMID: 7534313
Identification of a novel heparin binding domain in RHAMM and evidence that it modifies *HA* mediated locomotion of ras-transformed cells. Yang B; Hall C L; Yang B L; Savani R C; Turley E A
Manitoba Institute of Cell Biology, University of Manitoba, Winnipeg, Canada.
Journal of cellular biochemistry (UNITED STATES) Dec 1994, 56 (4) p455-68, ISSN 0730-2312 Journal Code: 8205768
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
We have previously reported that the hyaluronan (*HA*) *receptor* RHAMM (Receptor for HA Mediated Motility) [Turley et al., 1991] contains two HA binding motifs located within a 35 amino acid region of its C-terminus end [Yang et al., 1993] and that HA stimulation of the motility of ras-transformed fibroblasts is mediated via its interaction with RHAMM. Here we show that RHAMM also contains binding sites for heparin (HP) and that interaction of HP with these sites can regulate the locomotion of ras-transformed fibroblasts. At low concentrations (0.01 mg/ml), HP inhibited HA-induced locomotion of ras-transformed cells in a manner independent of RHAMM. At higher, but still physiological concentrations (0.1 mg/ml), HP alone stimulated cell locomotion and this stimulation appeared to be RHAMM-dependent as it was blocked by anti-RHAMM antibodies. Other related glycosaminoglycans such as chondroitin sulfate and dermatin sulfate had no effect on cell motility. In ligand blotting assays, GST-RHAMM fusion protein was shown to bind biotin-labelled HP and this binding was displaceable with unlabelled HP. In similar ligand binding analyses conducted with truncations of RHAMM fusion protein, the HP binding region was found to be localized in the same 35 amino acid segment of RHAMM that contains the two HA binding domains. Synthetic peptides corresponding to these HA binding domains were retained on and bound effectively to an HP-Sepharose affinity column. Fusion proteins generated by linkage of these peptides to the non-HP binding amino terminus of RHAMM conferred HP binding capacity to the genetically engineered proteins. Conversely, deletion of the HA binding domains of RHAMM resulted in fusion proteins devoid of HP binding activity. The relative affinities of RHAMM for HA and HP, as determined by competition and transblot assays as well as quantification of binding at various salt concentrations, indicated that RHAMM had lower affinity for HP than that for HA. These results demonstrate the existence of a new HP binding motif that has biological relevance to cell locomotion.

7/3,AB/76 (Item 76 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

08382650 95146149 PMID: 7531178
Astrocyte and microglial motility in vitro is functionally dependent on the *hyaluronan* *receptor* RHAMM.
Turley E A; Hossain M Z; Sorokan T; Jordan L M; Nagy J I Department of Physiology, University of Manitoba, Winnipeg, Canada. Glia (UNITED STATES) Sep 1994, 12 (1) p68-80, ISSN 0894-1491 Journal Code: 8806785
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
RHAMM (Receptor for Hyaluronic Acid Mediated Motility) has been identified as a receptor for the extracellular matrix component hyaluronan (HA) and was recently shown to be essential for the locomotion of normal and transformed peripheral cells. Until now the potential role of RHAMM in the motility of neural-derived cells has not been investigated. Here, we report that cultured primary astrocytes, astrocyte cell lines, and microglia express this receptor and exhibit RHAMM-dependent motility. Immunocytochemical localization of RHAMM showed that it was often present as aggregates at the periphery of cells in contact with one another or concentrated on protruding processes of isolated cells. Glial cells contained 50 and 72 kDa forms of RHAMM, and both of these forms were found to have HA binding capacity. Time lapse imaging of cell locomotion revealed a significant inhibition of motility and process elongation by neutralizing anti-RHAMM antibodies and by peptides corresponding to the HA binding domains of RHAMM. These results demonstrate that RHAMM serves a role in glial cell locomotion in vitro and provide the basis for investigations of the motile behavior of glial cells in vivo after CNS injury.

7/3,AB/77 (Item 77 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

08368242 95123446 PMID: 7529827
Requirement of the *hyaluronan* *receptor* RHAMM in neurite extension and motility as demonstrated in primary neurons and neuronal cell lines.
Nagy J I; Hacking J; Frankenstein U N; Turley E A
Department of Physiology, University of Manitoba, Winnipeg, Canada. Journal of neuroscience : the official journal of the Society for Neuroscience (UNITED STATES) Jan 1995, 15 (1 Pt 1) p241-52, ISSN 0270-6474 Journal Code: 8102140

Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
The recently cloned and characterized hyaluronan (*HA*) *receptor* RHAMM (receptor for HA-mediated motility) has been shown to play a critical role in mechanisms underlying the motile capacity of a variety of peripheral cell types. Similarities in molecular processes that govern cell locomotion and growth cone migration prompted us to investigate whether RHAMM also contributes to neurite migration in vitro. In immunohistochemical studies of PC12 cells, NG108-15 cells and a neuroblastoma/spinal cord neuronal hybrid cell line (NSC-34 cells) as well as rat and human primary neurons, a punctiform RHAMM labeling pattern was detected in cell bodies, along processes, and at growth cones. By Western blot analysis, the cells lines expressed major RHAMM forms with apparent MW of 60, 75, and 116 kDa. Treatment of NG108-15 cells with dibutyryl-cAMP led to a clear increase in immunolabeling for RHAMM and enhanced expression of the 60 and 75 kDa forms. A polyclonal anti-RHAMM antibody that interferes with HA/RHAMM interaction significantly reduced neurite migration of each cell type examined, while another directed against a RHAMM repeat sequence thought to promote RHAMM receptor aggregation significantly stimulated neurite migration of NSC-34 and rat primary neurons. Different monoclonal anti-RHAMM antibodies had differential inhibitory actions on neurite movement. Low concentrations (ng/ml) of a peptide corresponding to an HA binding domain within RHAMM inhibited neurite migration. These results are the first to implicate RHAMM in the mediation of neurite motility and migration and to point to the potential importance of HA in this process.

7/3,AB/78 (Item 78 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

08351904 95111345 PMID: 7529076
RHAMM, a receptor for *hyaluronan*-mediated motility, on normal human lymphocytes, thymocytes and malignant B cells: a mediator in B cell malignancy?
Pilarski L M; Masellis-Smith A; Belch A R; Yang B; Savani R C; Turley E A Department of Immunology, University of Alberta, Edmonton, Canada. Leukemia & lymphoma (SWITZERLAND) Aug 1994, 14 (5-6) p363-74, ISSN 1042-8194 Journal Code: 9007422
Document type: Journal Article; Review; Review, Tutorial
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
RHAMM (Receptor for HA Mediated Motility) is a novel *HA* *receptor* that has been linked to regulating cell locomotion and density dependent contact inhibition of fibroblasts, smooth muscle cells, macrophages, lymphocytes, astrocytes and sperm. The ubiquitous expression of RHAMM suggests the existence of multiple isoforms, and indeed, RHAMM is found in various cellular compartments, namely nuclear, cytosolic, membrane-bound and extracellular. In this review, we emphasize the evolving role of RHAMM in B cell malignancies, and examine the function of RHAMM in T cell development in the thymic microenvironment. Both the motile behaviour of progenitor thymocytes (CD3-CD4-CD8-) and malignant B cells from multiple myeloma (MM), plasma cell leukemia, and hairy cell leukemia was blocked by monoclonal antibodies to RHAMM, suggesting that motility may correlate with increased expression of RHAMM at the cell surface. Interestingly, the soluble form of RHAMM is able to inhibit fibroblast locomotion, and it is likely that a balance between expression of both forms determines, in part the motility of cells. RHAMM appears to play a fundamental role in the immune system and the ability of RHAMM to function as a motility receptor is likely to be due to complex variables including the extent to which soluble RHAMM is secreted. RHAMM expression characterizes circulating monoclonal B cells as abnormal. potentially invasive and/or metastatic components of myeloma and may underlie the malignant behavior of these cells.

7/3,AB/79 (Item 79 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

08317013 95073991 PMID: 7527024
Intercellular adhesion molecule-1 is a cell surface receptor for *hyaluronan*.
McCourt P A; Ek B; Forsberg N; Gustafson S
Department of Medical and Physiological Chemistry, University of Uppsala, Sweden.
Journal of biological chemistry (UNITED STATES) Dec 2 1994, 269 (48) p30081-4, ISSN 0021-9258 Journal Code: 2985121R
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
Our laboratory has previously characterized and purified the *hyaluronan* *receptor* by hyaluronan affinity chromatography of rat liver endothelial cells. We have now isolated the receptor from whole rat liver and have obtained sufficient quantities for amino acid sequence analysis. Four peptides of various lengths were obtained from affinity-purified receptor and found to have identity with rat intercellular adhesion molecule-1. This glycoprotein is normally expressed in low amounts on the endothelial cells, but is up-regulated in inflamed and malignant tissues, and mediates cell-cell

adhesion as a ligand for lymphocyte function-associated antigen-1 and the macrophage-associated Mac-1. The affinity of intercellular adhesion molecule-1 for hyaluronan is likely to have important implications for cell adhesion in normal and in disease states such as inflammation, atherosclerosis, and cancer.

7/3,AB/80 (Item 80 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

08295163 95053378 PMID: 7525818
Hyaluronan *receptor* (CD44) expression and function in human peripheral blood monocytes and alveolar macrophages.
Culty M; O'Mara T E; Underhill C B; Yeager H; Swartz R P Department of Cell Biology, Georgetown University Medical Center, Washington, DC 20007.
Journal of leukocyte biology (UNITED STATES) Nov 1994, 56 (5) p605-11, ISSN 0741-5400 Journal Code: 8405628
Contract/Grant No.: HL41565; HL; NHLBI
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
CD44 glycoproteins are present on the surfaces of many hematopoietic cells and in some cases can bind hyaluronan, a major component of the extracellular matrix. In the present study, we have found that newly explanted human peripheral blood monocytes (PBMs) exhibit a major CD44 band of 85 kDa, whereas autologous alveolar macrophages (AM phi) express multiple isoforms ranging from 85 to 200 kDa. Within 4 h in culture, PBMs began expressing new CD44 isoforms of 120, 150, and 180 kDa. Newly explanted AM phi specifically bound [3H]hyaluronan (135 cpm/microgram protein), but newly explanted PBMs did not. However, in vitro cultured PBM progressively acquired the ability to bind [3H]hyaluronan and exhibited specific binding of hyaluronan similar to that of AM phi (113 cpm/microgram protein) after 4 days in culture. In both case, the binding of [3H]hyaluronan was specifically inhibited by the addition of monoclonal antibody directed against CD44. AM phi readily degraded [3H]hyaluronan and reached a plateau after 4 days in culture (115 cpm/microgram protein). Newly explanted PBM exhibit no hyaluronan degradation and only a small degradative activity after 4 days in culture (6 to 11 cpm/microgram protein). Thus, CD44 expression and function appear to change as PBM mature in vitro resembling more that found in AM phi.

7/3,AB/81 (Item 81 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

08276275 95035186 PMID: 7524689
Biotinylated *hyaluronic* acid: a new tool for probing hyaluronate-receptor interactions.
Pouyani T; Prestwich G D
Department of Chemistry, University at Stony Brook, New York 11794-3400. Bioconjugate chemistry (UNITED STATES) Jul-Aug 1994, 5 (4) p370-2, ISSN 1043-1802 Journal Code: 9010319
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
Hyaluronic acid (HA) is a linear polysaccharide composed of repeating disaccharide units of D-glucuronic acid (GlcUA) and N-acetyl-D-glucosamine (GlcNAc). Hyaluronate plays an important role in many biological processes as mediated by its interactions with a number of HA-binding proteins (the "hyaladherins") and with the cell surface *HA*-*receptor*, CD44. Studies of hyaluronate-hyaladherin interactions would be greatly facilitated by the availability of molecular probes derived from HA. We recently reported a convenient chemical modification of hyaluronate that introduces multiple pendant amine functionalities onto the HA carboxylate residues. We now report the preparation of biotinylated hyaluronic acid (molecular weight = 1.2 x 10(6) Da) as a probe for histochemical and immunochemical characterization of HA-binding proteins. Approximately one-third of the available HA glucuronate residues could be readily biotinylated in high molecular weight HA.

7/3,AB/82 (Item 82 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

08258541 95015780 PMID: 7523491
Distribution of *hyaluronan* in bull reproductive organs.
Tammi R; Ronkko S; Agren U M; Tammi M
Department of Anatomy, University of Kuopio, Finland.
journal of histochemistry and cytochemistry : official journal of the Histochemistry Society (UNITED STATES) Nov 1994, 42 (11) p1479-86, ISSN 0022-1554 Journal Code: 9815334
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
To study the expression of hyaluronan in male reproductive organs and the origin of seminal plasma hyaluronan, we stained various parts of the bull reproductive tract for hyaluronan using a biotinylated probe derived from cartilage proteoglycan (bHABC). The potential loss of hyaluronan during tissue processing was checked with a novel technique by blotting frozen tissue sections on nitrocellulose and staining the blots

with bHABC. In the same tissues the CD44 receptor was visualized by Hermes 1 antibody. The testes showed only traces of hyaluronan, whereas both the epithelium and the connective tissue of seminal vesicle, prostate, Cowper's gland, and epididymis were positive in bHABC staining. Hyaluronan was localized on the basolateral surfaces of these epithelial cells. The secretions inside the seminal vesicle and in the ducts of prostate and Cowper's gland were HA-positive, whereas the luminal contents of seminiferous tubules and epididymis were unstained both in paraffin sections and in the in situ blocks. The data indicate that hyaluronan in seminal plasma originates from the accessory sex glands. The co-localization of CD44 with hyaluronan in the basolateral surfaces of the accessory gland epithelia and its absence from other epithelia with little or no hyaluronan supports its role as a *hyaluronan* *receptor*.

7/3,AB/83 (Item 83 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

08183598 94320091 PMID: 7519123
Hyaluronan receptors are expressed on human malignant mesothelioma cells but not on normal mesothelial cells.
Asplund T; Heldin P
Department of Medical and Physiological Chemistry, University of Uppsala, Sweden.
Cancer research (UNITED STATES) Aug 15 1994, 54 (16) p4516-23, ISSN 0008-5472 Journal Code: 2984705R
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
Hyaluronan-binding sites were demonstrated on the cell surface of three malignant mesothelioma cell lines derived from human tumors using either [3H]hyaluronan or fluorescein-tagged hyaluronan. No hyaluronan-binding activity was observed on normal human mesothelial cells. The absence of hyaluronan receptors on normal human mesothelial cells was not due to a down-regulation by endogenously synthesized hyaluronan, since no binding sites appeared when the cells were cultured under conditions known to suppress hyaluronan synthesis (in starvation medium containing either hydrocortisone or n-butyrate) or to degrade endogenously synthesized hyaluronan (in the presence of Streptomyces or testicular hyaluronidase). The binding of [3H]hyaluronan on mesothelioma cells could be partially inhibited by prior incubation of the cells with trypsin, indicating that the hyaluronan-binding site is a protein. The binding sites on human malignant mesothelioma cells were shown to be saturable with about 54,000 hyaluronan molecules (M(r) 1.4 x 10(6)) bound per cell with a Kd of 0.3 x 10(-9) M. The binding was specific for hyaluronan inasmuch as a number of other macromolecules gave negligible inhibition of the binding. High molecular weight preparations of hyaluronan inhibited the binding more effectively than low molecular weight preparations; hyaluronan oligosaccharides down to a length of six monosaccharide units showed competing activity. The *hyaluronan* *receptor* appeared to be related to CD44 (a cell surface glycoprotein previously suggested to function as a *hyaluronan* *receptor*) since Hermes-1 monoclonal antibodies which inhibit the binding of hyaluronan to CD44 blocked a major part of the binding of hyaluronan to the mesothelioma cells. However, there was no strict correlation between the hyaluronan-binding activity on the mesothelioma cell lines tested and the levels of CD44 molecules on their cell surface, suggesting that only a subfraction of the CD44 molecules bound hyaluronan or that other hyaluronan-binding proteins also exist on those cells. The presence of hyaluronan receptors on mesothelioma cells, but not on their normal counterparts, may be of importance for the migration of the transformed cells in hyaluronan-enriched matrices and for their ability to form metastases.

7/3,AB/84 (Item 84 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

08173812 94308286 PMID: 7518470
Hyaluronan and the *hyaluronan* *receptor* RHAMM promote focal adhesion turnover and transient tyrosine kinase activity. Hall C L; Wang C; Lange L A; Turley E A
Department of Pediatrics, University of Manitoba, Winnipeg, Canada. Journal of cell biology (UNITED STATES) Jul 1994, 126 (2) p575-88, ISSN 0021-9525 Journal Code: 0375356
Contract/Grant No.: CA 51540; CA; NCI
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
The molecular mechanisms whereby hyaluronan (HA) stimulates cell motility was investigated in a C-H-ras transformed 10T 1/2 fibroblast cell line (C3). A significant ($p < 0.001$) stimulation of C3 cell motility with HA (10 ng/ml) was accompanied by an increase in protein tyrosine phosphorylation as detected by anti-phosphotyrosine antibodies using immunoblot analysis and immunofluorescence staining of cells. Tyrosine phosphorylation of several proteins was found to be both rapid and transient with phosphorylation occurring within 1 min of HA addition and dissipating below control levels 10-15 min later. These responses were also

elicited by an antibody generated against a peptide sequence within the *HA* *receptor* RHAMM. Treatment of cells with tyrosine kinase inhibitors (genistein, 10 micrograms/ml or herbimycin A, 0.5 micrograms/ml) or microinjection of anti-phosphotyrosine antibodies inhibited the transient protein tyrosine phosphorylation in response to HA as well as prevented HA stimulation of cell motility. To determine a link between HA-stimulated tyrosine phosphorylation and the resulting cell locomotion, cytoskeletal reorganization was examined in C3 cells plated on fibronectin and treated with HA or anti-RHAMM antibody. These agents caused a rapid assembly and disassembly of focal adhesions as revealed by immunofluorescent localization of vinculin. The time course with which HA and antibody induced focal adhesion turnover exactly paralleled the induction of transient protein tyrosine phosphorylation. In addition, phosphotyrosine staining colocalized with vinculin within structures in the lamellapodia of these cells. Notably, the focal adhesion kinase, pp125FAK, was rapidly phosphorylated and dephosphorylated after HA stimulation. These results suggest that HA stimulates locomotion via a rapid and transient protein tyrosine kinase signaling event mediated by RHAMM. They also provide a possible molecular basis for focal adhesion turnover, a process that is critical for cell locomotion.

7/3,AB/85 (Item 85 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

08141468 94275395 PMID: 7516415
Hyaluronan binding function of CD44 is transiently activated on T cells during an in vivo immune response.
Lesley J; Howes N; Perschl A; Hyman R
Department of Cancer Biology, Salk Institute, San Diego, California 92186-5800.
Journal of experimental medicine (UNITED STATES) Jul 1 1994, 180 (1) p383-7, ISSN 0022-1007 Journal Code: 2985109R
Contract/Grant No.: AI-31613; AI; NIAID; CA-14195; CA; NCI; CA-17733; CA; NCI
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
Though CD44 functions as a cell surface receptor for hyaluronan (HA) in some cell lines, most normal hematopoietic cells expressing CD44 do not bind HA. Certain CD44-specific monoclonal antibodies (mAbs) can rapidly induce CD44-mediated HA binding in normal murine T cells. This observation suggests that in vivo mechanisms may exist for activating the *HA* *receptor* function of CD44 on normal T cells. Here, it is shown that up to one third of splenic T cells are capable of CD44-mediated binding of fluorescein-conjugated HA (Fl-HA) during an in vivo allogeneic response. HA binding activity peaks at 7-8 d postinjection and declines rapidly. These rapid kinetics could be the result of transient activation of CD44 function and/or differentiation or expansion of short-lived population(s) that have constitutive HA-binding function. Both CD4 and CD8 T cells are included in the HA binding population which is strongly CD44 positive. After separation of HA-binding cells from nonbinding cells by cell sorting, it is shown that almost all cytotoxic effector cells are found in the HA-binding population. However, there is no evidence that CD44-mediated HA recognition is directly involved in the killing of target cells, since cytotoxicity could not be inhibited by CD44-specific mAbs that inhibit HA binding or by soluble HA. PCR amplification of cDNA reverse transcribed from RNA of sorted HA-binding cells indicated no evidence for CD44 isoforms other than the standard (hematopoietic) form. Though CD44 expression is known to be elevated upon T cell activation, and, as shown here, HA-binding function is induced in a portion of CD44-expressing T cells including cytotoxic effector cells, the role of CD44 and HA-recognition in immune responses is not known.

7/3,AB/86 (Item 86 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

08090351 94229273 PMID: 7513657
The regulation of sperm motility by a novel *hyaluronan* *receptor*.
Kornovski B S; McCoshen J; Kredentser J; Turley E
Department of Pediatrics, Manitoba Institute of Cell Biology, Winnipeg, Canada.
Fertility and sterility (UNITED STATES) May 1994, 61 (5) p935-40, ISSN 0015-0282 Journal Code: 0372772
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
OBJECTIVE: To determine if a novel receptor for hyaluronan, termed RHAMM, is responsible for the previously observed increase in sperm locomotion in response to hyaluronan and to assess whether expression of the RHAMM protein is involved in sperm motility. DESIGN: The RHAMM protein was localized on human sperm by immunofluorescence of fixed cells, fluorescence-activated cell sorter (FACS) of cell surface phenotype, and Western transblot analysis of cell proteins. The effect of monospecific antibodies on sperm motility was examined using computer-assisted image analysis. Results of motility studies were assessed statistically with analysis of variance.

SETTING: Samples were collected from donors from the University of Manitoba donor insemination program. SUBJECTS: Semen was collected twice from four participants and a total of 10,000 sperm per sample were evaluated. RESULTS: A *hyaluronan* *receptor*, RHAMM, was localized by immunofluorescence along the tail, the midpiece, and the head of sperm. Positive staining obtained with FACS analysis indicated that RHAMM occurred on the surface of sperm, whereas immunoblot analysis of sperm cell lysates revealed RHAMM proteins of MWE 58 and 64 kd, consistent with the size of RHAMM localized from fibroblasts. A polyclonal antibody specific to a peptide encoded in the fibroblast RHAMM complementary DNA significantly decreased the motility of sperm. Analysis of this inhibition is consistent with an effect of the antibody on flagellar function. CONCLUSIONS: The presence of RHAMM on sperm surfaces and the ability of monospecific antibodies to inhibit sperm motility suggest an important role for this novel glycoprotein in sperm motility.

7/3,AB/87 (Item 87 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

08048875 94199973 PMID: 7512013
Identification of *hyaluronan* binding proteins using a biotinylated *hyaluronan* probe.
Hoare K; Savani R C; Wang C; Yang B; Turley E A
Department of Pediatrics and Child Health, Manitoba Institute of Cell Biology, Winnipeg, Canada.
Connective tissue research (ENGLAND) 1993, 30 (2) p117-26, ISSN 0300-8207 Journal Code: 0365263
Contract/Grant No.: CA 51540; CA; NCI
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
A method for detecting hyaluronan (HA)-binding proteins in transblot assays using biotinylated HA (BHA) is described. Some of the binding characteristics of a novel *HA* *receptor* termed RHAMM (Receptor for HA-Mediated Motility) are characterized using this assay. The method is also used to detect other HA-binding proteins in tissue homogenates. This method is semiquantitative, rapid, reproducible, sensitive and therefore of potential use in identifying the levels of HA-binding proteins in different cells and tissues.

7/3,AB/88 (Item 88 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

08025432 94147973 PMID: 7508860
Identification of a common *hyaluronan* binding motif in the *hyaluronan* binding proteins RHAMM, CD44 and link protein. Yang B; Yang B L; Savani R C; Turley E A
Manitoba Institute of Cell Biology, University of Manitoba, Winnipeg, Canada.
EMBO journal (ENGLAND) Jan 15 1994, 13 (2) p286-96, ISSN 0261-4189 Journal Code: 8208664
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
We have previously identified two hyaluronan (HA) binding domains in the *HA* *receptor* , RHAMM, that occur near the carboxyl-terminus of this protein. We show here that these two HA binding domains are the only HA binding regions in RHAMM, and that they contribute approximately equally to the HA binding ability of this receptor. Mutation of domain II using recombinant polypeptides of RHAMM demonstrates that K423 and R431, spaced seven amino acids apart, are critical for HA binding activity. Domain I contains two sets of two basic amino acids, each spaced seven residues apart, and mutation of these basic amino acids reduced their binding to HA--Sepharose. These results predict that two basic amino acids flanking a seven amino acid stretch [hereafter called B(X7)B] are minimally required for HA binding activity. To assess whether this motif predicts HA binding in the intact RHAMM protein, we mutated all basic amino acids in domains I and II that form part of these motifs using site-directed mutagenesis and prepared fusion protein from the mutated cDNA. The altered RHAMM protein did not bind HA, confirming that the basic amino acids and their spacing are critical for binding. A specific requirement for arginine or lysine residues was identified since mutation of K430, R431 and K432 to histidine residues abolished binding. Clustering of basic amino acids either within or at either end of the motif enhanced HA binding activity while the occurrence of acidic residues between the basic amino acids reduced binding. The B(X7)B motif, in which B is either R or K and X7 contains no acidic residues and at least one basic amino acid, was found in all HA binding proteins molecularly characterized to date. Recombinant techniques were used to generate chimeric proteins containing either the B(X7)B motifs present in CD44 or link protein, with the amino-terminus of RHAMM (amino acids 1-238) that does not bind HA. All chimeric proteins containing the motif bound HA in transblot analyses. Site-directed mutations of these motifs in CD44 sequences abolished HA binding. Collectively, these results predict that the motif of B(X7)B as a minimal binding requirement for HA in RHAMM, CD44 and link protein, and occurs in all HA binding proteins described to date.

7/3,AB/89 (Item 89 from file: 155)

DIALOG(R)File 155:MEDLINE(R)

07981838 94116435 PMID: 7507029
Restricted expression of the *hyaluronan* *receptor*, CD44, during postimplantation mouse embryogenesis suggests key roles in tissue formation and patterning.
Wheatley S C; Isacke C M; Crossley P H
Department of Biology, Imperial College of Science, Technology and Medicine, London, UK.
Development (Cambridge, England) (ENGLAND) Oct 1993, 119 (2) p295-306, ISSN 0950-1991 Journal Code: 8701744
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
CD44 is a multifunctional adhesion protein that acts as a major receptor for the hygroscopic extracellular matrix component, hyaluronan. This receptor-ligand binding directly mediates at least some of the cell-cell and cell-matrix interactions ascribed to CD44. Other interactions involving CD44 may be modulated indirectly by its ability to bind growth factors and thereby to promote cell attachment. During vertebrate development, multiple cases of hyaluronan involvement in cell proliferation, cell migration and histogenesis have been documented. In addition, there is evidence suggesting a central role for cell surface glycoproteins and proteoglycans in mediating the action of polypeptide growth factors involved in tissue patterning. In view of this, we undertook to investigate expression of the CD44 protein during postimplantation mouse embryogenesis. Between 9.5 and 12.5 days of embryonic development, the predominant form of CD44 protein corresponds to the hyaluronan-binding CD44H form. However, species with a higher M(r) were also detected, implying that CD44 isoforms generated by alternative splicing of CD44 RNA are employed in normal development. Further, we used mouse embryos to perform whole-mount immunohistochemistry and examine the temporal and spatial distribution of this glycoprotein. CD44 is expressed at high levels in the heart, somites and condensing limb-bud mesenchyme at critical stages of morphogenesis. These sites correlate with regions where hyaluronan has been demonstrated to regulate morphogenetic events. Of novel interest, however, is the high expression of CD44 in regions that do not correlate with sites of known hyaluronan-mediated developmental events. These include instructive epithelia participating in epithelial-mesenchymal cell interactions such as the apical ectodermal ridge of the developing limb bud and the odontogenic placodes of the presumptive upper and lower jaws.

7/3,AB/90 (Item 90 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

07959864 94095669 PMID: 7505784
Internalization of *hyaluronan* by chondrocytes occurs via receptor-mediated endocytosis.
Hua Q; Knudson C B; Knudson W
Department of Biochemistry, Rush-Presbyterian-St. Luke's Medical Center, Chicago, Illinois 60612.
Journal of cell science (ENGLAND) Sep 1993, 106 (Pt 1) p365-75, ISSN 0021-9533 Journal Code: 0052457
Contract/Grant No.: AR39239; AR; NIAMS; AR39507; AR; NIAMS Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
Several studies have suggested that chondrocytes must have the capacity to internalize and degrade extracellular hyaluronan. In the present study we show direct evidence that hyaluronan is, in fact, endocytosed by chondrocytes and that the endocytosis is mediated via cell surface CD44/hyaluronan receptors. Cultures of bovine articular chondrocytes as well as rat chondrosarcoma chondrocytes were incubated with either fluorescein- or 3H-labeled hyaluronan. Intense binding and accumulation of labeled hyaluronan was visualized by fluorescence microscopy or bright-field/dark-field microscopy following autoradiography. Cell surface hyaluronan was removed with either trypsin or Streptomyces hyaluronidase in order to distinguish and quantify intracellular endocytosed hyaluronan. Labeled hyaluronan was visualized within small discrete intracellular vesicles distributed throughout the cytoplasm. Binding and endocytosis of fluorescein- or 3H-labeled hyaluronan was totally blocked by the addition of excess unlabeled hyaluronan or hyaluronan hexasaccharides, competitive inhibitors of hyaluronan/*hyaluronan* *receptor* interactions. Binding and endocytosis was also blocked by the addition of anti-CD44 monoclonal antibodies. Characterization of endocytosed 3H-labeled hyaluronan demonstrated that a significant portion of the hyaluronan was degraded by both the bovine articular and rat chondrosarcoma chondrocytes. Interestingly, a higher proportion of bound hyaluronan was internalized by the bovine chondrocytes. Therefore, *hyaluronan* *receptor* -mediated endocytosis and degradation of hyaluronan may provide a critical link to the maintenance and homeostasis of cartilage tissue.

7/3,AB/91 (Item 91 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

07944149 94081314 PMID: 7505012
Hyaluronic acid-induced lymphocyte signal

transduction and *HA* *receptor* (GP85/CD44)-cytoskeleton interaction.
Bourguignon L Y; Lokeshwar V B; Chen X; Kerrick W G
Department of Cell Biology and Anatomy, University of Miami Medical School, FL 33101.
Journal of immunology (Baltimore, Md. : 1950) (UNITED STATES) Dec 15 1993, 151 (12) p6634-44, ISSN 0022-1767 Journal Code: 2985117R
Contract/Grant No.: 1F32CA06057; CA; NCI; GM 36353; GM; NIGMS Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
The purposes of this study are to characterize the binding of hyaluronic acid (HA) to mouse T lymphoma cells, to measure changes in intracellular Ca2+ after HA binding, to elucidate the interaction between the *HA* *receptor* , GP85(CD44), and ankyrin in the membrane skeleton, and finally to correlate these events with *HA* *receptor* patching/capping and cell adhesion to HA. First, we established an in vivo assay using [3H]HA to measure the binding of HA to mouse T lymphoma cells, and found that the binding of [3H]HA to these cells is readily inhibited by the addition of anti-GP85(CD44) antibody suggesting that GP85(CD44) is the *HA* *receptor* . Next, we examined various signal transducing events that occur after HA binds to its receptor on mouse T lymphoma cells. The results of these studies indicate that the concentration of intracellular Ca2+ (as measured by Fura-2 fluorescence) begins to increase within seconds, and reaches a maximal level 5 min after the addition of HA to the cells. After this increase of intracellular Ca2+, HA induces both its receptors, GP85(CD44), to form patched/capped structures, and cell adhesion to HA-coated plates. Furthermore, we have determined that GP85(CD44) binds directly and specifically to ankyrin (Kd approximately 1.94 nM) in a saturable manner; and that ankyrin is preferentially accumulated underneath the HA-induced GP85(CD44) capped structures. The Ca2+ ionophore, ionomycin, was found to stimulate HA-induced receptor capping and adhesion while EGTA (a Ca2+ chelator), nefedipine/bepridil (Ca2+ channel blockers), W-7 (a calmodulin antagonist), and cytochalasin D (a microfilament inhibitor), but not colchicine (a microtubule disrupting agent), inhibit HA-induced receptor redistribution and adhesion to HA-coated plates. These findings strongly suggest that ankyrin plays an important role in linking the *HA* *receptor*, GP85(CD44), to the membrane-associated actomyosin contractile system during hyaluronic acid-mediated lymphocyte activation.

7/3,AB/92 (Item 92 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

07930234 94065240 PMID: 7504026
Hyaluronan is inversely correlated with the expression of CD44 in the dermal condensation of the embryonic hair follicle.
Underhill C B
Department of Anatomy and Cell Biology, Georgetown Medical Center, Washington, DC 20007.
Journal of investigative dermatology (UNITED STATES) Dec 1993, 101 (6) p820-6, ISSN 0022-202X Journal Code: 0426720
Contract/Grant No.: HD17664; HD; NICHD; HD26758; HD; NICHD Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
Previously, we have shown that CD44 (the *hyaluronan* *receptor*) was involved in the degradation of hyaluronan. In the present study, we examined the distribution of CD44 and hyaluronan in the skin of embryonic and mature mice. During embryonic development, CD44 was prominently expressed by the condensed mesenchymal cells involved in the formation of the hair follicles, but was absent from the surrounding interstitial cells. The cells of the dermal condensation expressed CD44 throughout the development of the hair follicle; however, once the hair follicle reached maturity, the mesenchymal cells of the dermal papilla no longer expressed this molecule. In contrast to the above, the distribution of hyaluronan was reversed from that of CD44. Hyaluronan was widespread throughout the embryonic dermis, but was conspicuously absent from the regions of the dermal condensation. This arrangement persisted through the development of the hair follicle; however, in the mature hair follicle, hyaluronan reappeared in the dermal papilla. Thus, in the embryonic dermis, the expression of CD44 and hyaluronan were complementary to each other. However, in the adult skin, only minor changes were detected in the levels of CD44 and hyaluronan associated with the cells of the dermal condensation during the hair cycle. When organ cultures of embryonic mouse skin were treated with Streptomyces hyaluronidase, the interstitial mesenchymal cells became compacted, indicating that the removal of hyaluronan leads to the condensation of these cells. The results of this study are consistent with the hypothesis that the expression of CD44 by the inductive mesenchymal cells allows them to degrade hyaluronan in a localized region, leading to formation and maintenance of the dermal condensation.

7/3,AB/93 (Item 93 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

07928430 94063332 PMID: 7694885
Localization of *hyaluronan* in mouse embryos during

implantation, gastrulation and organogenesis.
Fenderson B A; Stamenkovic I; Aruffo A
Department of Pathology and Cell Biology, Thomas Jefferson University, Philadelphia, PA 19107.
Differentiation; research in biological diversity (GERMANY) Sep 1993, 54 (2) p85-98, ISSN 0301-4681 Journal Code: 0401650
Contract/Grant No.: CA 55735; CA; NCI
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
Hyaluronan was localized in postimplantation mouse embryos using CD44, the principal *hyaluronan* *receptor* . The specificity of CD44 receptor-globulin labelling was confirmed using Streptomyces hyaluronidase, anti-chondroitin sulfate antibody, and other receptor globulins. Our major findings are summarized as follows: 1. Implantation of the blastocyst into the uterine wall triggers a rapid loss of hyaluronan from the extracellular matrix of decidual cells on the anti-mesometrial side of the uterus. 2. Hyaluronan appears early in development in the yolk cavity, and the basement membranes of primitive ectoderm and primitive endoderm. 3. During gastrulation, mesodermal cells enter a hyaluronan-rich environment, but lack a pericellular hyaluronan coat themselves. 4. In limb bud embryos, hyaluronan is present throughout the cranial mesenchyme, but is generally not present in the branchial bars, somites, or limb buds. 5. At mid-gestation, hyaluronan is present in the axial skeleton, craniofacial mesenchyme, endocardial cushions of the heart, smooth muscle of the gastrointestinal tract, and connective tissue throughout the body. The pattern of hyaluronan expression in the day 13 fetus is nearly identical to the published distribution of transforming growth factor beta (TGF beta), suggesting a close functional relationship between these molecules. Together, the results suggest that hyaluronan is involved in the formation of early mesoderm, differentiation of craniofacial mesenchyme, and morphogenesis of the axial skeleton.

7/3,AB/94 (Item 94 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

07906794 94043455 PMID: 7693717
TGF-beta 1 stimulation of cell locomotion utilizes the *hyaluronan* *receptor* RHAMM and *hyaluronan*.
Samuel S K; Hurta R A; Spearman M A; Wright J A; Turley E A; Greenberg A H
Manitoba Institute of Cell Biology, University of Manitoba, Winnipeg, Canada.
Journal of cell biology (UNITED STATES) Nov 1993, 123 (3) p749-58, ISSN 0021-9525 Journal Code: 0375356
Contract/Grant No.: CA51540; CA; NCI
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
TGF-beta is a potent stimulator of motility in a variety of cell types. It has recently been shown that hyaluronan (HA) can directly promote locomotion of cells through interaction with the *HA* *receptor* RHAMM. We have investigated the role of RHAMM and HA in TGF-beta-stimulated locomotion and show that TGF-beta triggers the transcription, synthesis and membrane expression of the RHAMM receptor and the secretion of HA coincident with the induction of the locomotory response. This was demonstrated by both incubating cells with exogenous TGF-beta 1 and by stimulating the production of bioactive TGF-beta 1 in tumor cells transfected with TGF-beta 1 under the control of the metallothionein promoter. TGF-beta 1-induced locomotion was suppressed by antibodies that prevented HA/RHAMM interaction, using polyclonal antibodies to either RHAMM fusion protein or RHAMM peptides, or mAbs to purified RHAMM. Peptides corresponding to the HA-binding motif of RHAMM also suppressed TGF-beta 1-induced increases in motility rate. Spontaneous locomotion of fibrosarcoma cells was blocked by neutralizing secreted TGF-beta with panspecific TGF-beta antibodies and by inhibition of TGF-beta 1 secretion with antisense oligonucleotides. Polyclonal anti-RHAMM fusion protein antibodies and peptide from the RHAMM HA-binding motif also suppressed the spontaneous motility rate of fibrosarcoma cells. These data suggest that fibrosarcoma cell locomotion requires TGF-beta, and the pathway by which TGF-beta stimulates locomotion uses the *HA* *receptor* RHAMM and HA.

7/3,AB/95 (Item 95 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

07872583 94010070 PMID: 7691670
Hyaluronan-binding proteins in development, tissue homeostasis, and disease.
Knudson C B; Knudson W
Department of Biochemistry, Rush-Presbyterian-St. Luke's Medical Center, Chicago, Illinois 60612.
FASEB journal : official publication of the Federation of American Societies for Experimental Biology (UNITED STATES) Oct 1993, 7 (13) p1233-41, ISSN 0892-6638 Journal Code: 8804484
Contract/Grant No.: AR39239; AR; NIAMS; AR39507; AR; NIAMS Document type: Journal Article; Review; Review, Tutorial Languages: ENGLISH
Main Citation Owner: NLM

Record type: Completed
The high molecular weight glycosaminoglycan hyaluronan plays an important role in tissue remodeling during development, normal tissue homeostasis, and disease. The interaction of hyaluronan with matrix hyaluronan-binding proteins and cell-surface hyaluronan receptors regulates many aspects of cell behavior such as cell migration, cell-cell adhesion, and cell differentiation. Hyaluronan-binding proteins have been grouped together as a family termed hyaladherins--further subdivided in matrix and cell-surface hyaladherins (receptors). Specific hyaluronan-hyaladherin interactions that affect cell behavior are the focus of this review. Both clearance and turnover of hyaluronan involve *hyaluronan* *receptor*-mediated endocytosis. Pericellular matrix assembly and retention on many cells, especially chondrocytes, are mediated by hyaluronan receptors, in coordination with other matrix hyaladherins. Hyaluronan can also have an independent, direct effect on cell-to-cell adhesion as well as migration, again mediated by specific cell-surface hyaluronan receptors. This is especially apparent in tumor cells, where metastatic potential is correlated with *hyaluronan* *receptor* expression. As migrating cells encounter new environments enriched in matrix hyaladherins, the capacity for matrix assembly may terminate cell migration. Thus, the temporal/spatial deposition of particular matrix hyaladherins also serves as signals or matrix cues to alter cell behavior.

7/3,AB/96 (Item 96 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

07814341 93345625 PMID: 7688314
Ras-transformed cells express both CD44 and RHAMM *hyaluronan* receptors: only RHAMM is essential for *hyaluronan* -promoted locomotion.
Turley E A; Austen L; Moore D; Hoare K
Manitoba Institute of Cell Biology, Winnipeg, Canada.
Experimental cell research (UNITED STATES) Aug 1993, 207 (2) p277-82 , ISSN 0014-4827 Journal Code: 0373226
Contract/Grant No.: CA51540; CA; NCI
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
Hyaluronan (HA) is an important regulator of cell locomotion. We show that ras-transformed cells, termed 245 cells, respond to HA with an increase in random locomotion. We show that two HA receptors, RHAMM (receptor for hyaluronan-mediated motility) and CD44, are present on these ras-transformed fibroblasts. RHAMM is expressed as a 58-kDa protein and is distributed primarily as patches over lamellae. CD44 occurs largely as an 85- to 90-kDa protein that is distributed more or less evenly over the cell surface with small amounts concentrated at the tips of lamellae. CD44 and RHAMM both bind biotinylated HA in a transblot assay, indicating that they are both potential fibroblast HA receptors. CD44 binds approximately five times more HA than RHAMM as determined by densitometric analysis of transblots, indicating that this protein is the major *HA* *receptor* on fibroblasts. We assessed the role of these receptors in mediating the stimulatory effects of HA on cell motility by using antibody neutralization. Several antibodies to CD44 were used that inhibit HA/CD44 interactions. None of these had an effect on locomotory responses to HA, indicating that CD44 is not directly involved in mediating locomotion in response to HA on ras-transformed cells. In contrast, antibodies specific to RHAMM completely inhibited locomotion, indicating that RHAMM is the primary mediator of HA-promoted locomotion of ras-transformed cells.

7/3,AB/97 (Item 97 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

07814305 93345589 PMID: 7688309
Antibody-induced activation of the *hyaluronan* *receptor* function of CD44 requires multivalent binding by antibody.
Lesley J; Kincade P W; Hyman R
Department of Cancer Biology, Salk Institute, San Diego, CA 92186-5800.
European journal of immunology (GERMANY) Aug 1993, 23 (8) p1902-9, ISSN 0014-2980 Journal Code: 1273201
Contract/Grant No.: AI-19884; AI; NIAID; AI-31613; AI; NIAID; CA-13287; CA; NCI; +
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
CD44 can function as a receptor for hyaluronan (HA). However, many cell lines and normal hematopoietic cells that express CD44 do not constitutively bind HA. A monoclonal antibody (mAb) specific for CD44 (IRAWB 14) has been described previously which induces CD44-mediated binding of HA rapidly (seconds to minutes) in some cell lines and in normal murine T cells. Of 16 CD44-specific mAb tested in the present study, only 3 exhibited this activity. Monovalent Fab fragments were prepared from two IgG2a antibodies that induce HA binding (IRAWB 14 and IRAWB 26) and used to determine whether multivalent binding was required for induction of *HA* *receptor* function. Fab from both antibodies had a tendency to form multivalent aggregates. After addition of iodoacetamide to prevent further aggregation, multimeric and monovalent forms were separated by gel filtration. This made it possible

to compare the inducing activity of monovalent and multivalent antibody fragments of identical composition in the absence of Fc determinants. Multimeric forms were very active at inducing binding of fluorescein-conjugated HA (Fl-HA). Monovalent Fab fragments of both antibodies had 20- to 50-fold lower binding activity than intact antibody or multimer. IRAWB 26 Fab monomers were completely inactive in the induction of HA-binding. The observed weak inducing activity of IRAWB 14 Fab monomer could be attributed to very low levels of contaminating multimer. Induction of HA binding could also be achieved by using anti-immunoglobulin to cross-link Fab monomers of IRAWB 26. Thus, multivalent binding was required for the activation of HA binding by CD44-specific antibody, suggesting that the distribution of CD44 molecules on the cell surface is important for *HA* *receptor* function. In kinetic studies, induction of *HA* *receptor* function occurred simultaneously with antibody binding at 0 degrees C (ice water bath). Furthermore, antibody could induce HA binding in paraformaldehyde-fixed cells, which were permeable to propidium iodide and trypan blue, suggesting that intracellular signaling mechanisms were not involved in induction of receptor function. We conclude, therefore, that these CD44-specific antibodies are inducing HA binding by directly influencing the distribution of CD44 on the cell surface. The possibility of a concurrent change in CD44 conformation is not ruled out. We discuss possible mechanisms by which CD44 might be activated to bind HA in vivo.

7/3,AB/98 (Item 98 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

07705339 93232012 PMID: 7682552
Identification of two *hyaluronan*-binding domains in the *hyaluronan* *receptor* RHAMM.
Yang B; Zhang L; Turley E A
Manitoba Institute of Cell Biology, University of Manitoba, Winnipeg, Canada.
Journal of biological chemistry (UNITED STATES) Apr 25 1993, 268 (12) p8617-23, ISSN 0021-9258 Journal Code: 2985121R
Contract/Grant No.: CA 51540; CA; NCI
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
We have identified two discrete hyaluronan- (HA) binding domains in the *HA* *receptor* RHAMM (Receptor for HA-Mediated Motility) that mediates the locomotion of H-ras transformed fibroblasts. A complete RHAMM cDNA (1.43 kilobases (kb)) was expressed as a fusion protein with pGEX-2T in Escherichia coli HB101 and was shown to bind specifically to both biotin-labeled HA in a transblot assay and to HA-Sepharose. The complete cDNA was truncated with restriction endonucleases from the 3' end resulting in 1.30-, 1.02-, 0.71-, and 0.41-kb cDNAs which were then expressed in HB101. Only the fusion peptide expressed from the complete cDNA and the 1.30-kb cDNA bound to HA indicating that the region located between 1.02-1.30 kb of RHAMM cDNA was critical for recognition of this glycosaminoglycan. Deletion of 114 bases in this region virtually eliminated HA binding activity thus defining the major glycosaminoglycan binding region to amino acids 400-434 located near the carboxyl terminus of RHAMM. Two domains containing clusters of basic amino acids were identified within this region. Synthetic peptides mimicking these two domains both inhibited HA binding to the complete 1.43-kb expressed glutathione s-transferase-RHAMM fusion protein, and also directly bound to HA-Sepharose. Random peptides and peptides mimicking other regions in RHAMM did not inhibit HA-RHAMM interactions and bound weakly to HA-Sepharose. Oligonucleotides encoding either of these two peptides were linked to the NH2-terminal 0.71 kb of RHAMM which encoded a peptide that did not contain HA binding activity. Fusion proteins containing either of these recombinant peptides acquired HA binding activity as assessed with a transblot assay. Thus, we have identified two domains within RHAMM that are responsible for its HA binding activity.

7/3,AB/99 (Item 99 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

07636474 93154675 PMID: 8428724
Hyaluronic acid uptake by the isolated, perfused rat liver: an index of hepatic sinusoidal endothelial cell function.
Deaciuc I V; Bagby G J; Lang C H; Spitzer J J
Department of Physiology, Louisiana State University Medical Center, New Orleans 70112.
Hepatology (Baltimore, Md.) (UNITED STATES) Feb 1993, 17 (2) p266-72 , ISSN 0270-9139 Journal Code: 8302946
Contract/Grant No.: GM 32654; GM; NIGMS
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
Previous studies indicate that sinusoidal endothelial cells bind and internalize hyaluronic acid at much greater rates than do other liver cells. Thus hepatic hyaluronic acid removal rate may be indicative of sinusoidal endothelial cell function. In these studies the uptake of hyaluronic acid (molecular weight 1.3 x 10(6)) was measured in isolated perfused rat liver under

a variety of conditions. Uptake was dependent on hyaluronic acid concentration. At all concentrations tested, the rate of hyaluronic acid uptake stabilized at a steady-state level 2 to 3 min after development of a high rate of apparent uptake. At saturating hyaluronic acid concentration (150 ng.ml-1), the steady-state uptake rate was 10.4 +/- 1.0 micrograms.gm-1 liver wet wt.hr-1, which is as high as or higher than the rates reported for isolated rat liver sinusoidal endothelial cells. The half-maximal rate of uptake was attained at a hyaluronic acid concentration of 80 ng.ml-1. Hyaluronic acid uptake was inhibited by heparin (80%), a competitive ligand for the *hyaluronic* *acid* *receptor* on sinusoidal endothelial cells; 4 beta-phorbol 12 beta-O-myristoyl 13 alpha-acetate (25% to 50%), a tumor promoter and activator of protein kinase C; prostaglandin F2 alpha (24% to 52%), an eicosanoid secreted in the liver by Kupffer cells; A23187 (33% to 66%), a Ca2+ ionophore; and Escherichia coli lipopolysaccharide (16% to 43%). Platelet activating factor did not affect hyaluronic acid uptake by the perfused liver. Hyaluronic acid uptake was increased by 50% after a 24-hr fast.(ABSTRACT TRUNCATED AT 250 WORDS)

7/3,AB/100 (Item 100 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

07633040 93147134 PMID: 7678838
Hyaluronan *receptor* -directed assembly of chondrocyte pericellular matrix.
Knudson C B
Department of Biochemistry, Rush-Presbyterian-St. Luke's Medical Center, Chicago, IL 60612.
Journal of cell biology (UNITED STATES) Feb 1993, 120 (3) p825-34, ISSN 0021-9525 Journal Code: 0375356
Contract/Grant No.: AR39239; AR; NIAMS; AR39507; AR; NIAMS Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
Initial assembly of extracellular matrix occurs within a zone immediately adjacent to the chondrocyte cell surface termed the cell-associated or pericellular matrix. Assembly within the pericellular matrix compartment requires specific cell-matrix interactions to occur, that are mediated via membrane receptors. The focus of this study is to elucidate the mechanisms of assembly and retention of the cartilage pericellular matrix proteoglycan aggregates important for matrix organization. Assembly of newly synthesized chondrocyte pericellular matrices was inhibited by the addition to hyaluronan hexasaccharides, competitive inhibitors of the binding of hyaluronan to its cell surface receptor. Fully assembled chondrocyte pericellular matrices were displaced using hyaluronan hexasaccharides as well. When exogenous hyaluronan was added to matrix-free chondrocytes in combination with aggrecan, a pericellular matrix equivalent in size to an endogenous matrix formed within 30 min of incubation. Addition of hyaluronan and aggrecan to glutaraldehyde-fixed chondrocytes resulted in matrix assembly comparable to live chondrocytes. These matrices could be inhibited from assembling by the addition of excess hyaluronan hexasaccharides or displaced once assembled by subsequent incubation with hyaluronan hexasaccharides. The results indicate that the aggrecanrich chondrocyte pericellular matrix is not only on a scaffolding of hyaluronan, but actually anchored to the cell surface via the interaction between hyaluronan and hyaluronan receptors.

7/3,AB/101 (Item 101 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

07596512 93123357 PMID: 1282514
CD44: the *hyaluronan* *receptor*.
Underhill C
Department of Anatomy and Cell Biology, Georgetown Medical Center, Washington DC 20007.
Journal of cell science (ENGLAND) Oct 1992, 103 (Pt 2) p293-8, ISSN 0021-9533 Journal Code: 0052457
Contract/Grant No.: HD26758; HD; NICHD; HL41565; HL; NHLBI Document type: Journal Article; Review; Review, Tutorial Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed

7/3,AB/102 (Item 102 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

07489109 93016882 PMID: 1401082
Cytokine regulation of human lung fibroblast *hyaluronan* (*hyaluronic* acid) production. Evidence for cytokine-regulated *hyaluronan* (*hyaluronic* acid) degradation and human lung fibroblast-derived hyaluronidase.
Sampson P M; Rochester C L; Freundlich B; Elias J A
Section of Pulmonary and Critical Care Medicine, Yale University School of Medicine, New Haven, Connecticut 06510.
Journal of clinical investigation (UNITED STATES) Oct 1992, 90 (4) p1492-503, ISSN 0021-9738 Journal Code: 7802877
Contract/Grant No.: HL-08805; HL; NHLBI; HL-36708; HL; NHLBI; HL-41216; HL; NHLBI
Document type: Journal Article
Languages: ENGLISH

Main Citation Owner: NLM
Record type: Completed
We characterized the mechanisms by which recombinant (r) tumor necrosis factor (TNF), IFN-gamma, and IL-1, alone and in combination, regulate human lung fibroblast hyaluronic acid (HA) production. Each cytokine stimulated fibroblast HA production. The combination of rTNF and rIFN-gamma resulted in a synergistic increase in the production of high molecular weight HA. This was due to a synergistic increase in hyaluronate synthetase activity and a simultaneous decrease in HA degradation. In contrast, when rTNF and rIL-1 were combined, an additive increase in low molecular weight HA was noted. This was due to a synergistic increase in hyaluronate synthetase activity and a simultaneous increase in HA degradation. Human lung fibroblasts contained a hyaluronidase that, at pH 3.7, depolymerized high molecular weight HA to 10-40 kD end products of digestion. However, hyaluronidase activity did not correlate with fibroblast HA degradation. Instead, HA degradation correlated with fibroblast-HA binding, which was increased by rIL-1 plus rTNF and decreased by rIFN-gamma plus rTNF. Recombinant IL-1 and rTNF weakly stimulated and rIL-1 and rTNF in combination further augmented the levels of CD44 mRNA in lung fibroblasts. In contrast, rIFN-gamma did not significantly alter the levels of CD44 mRNA in unstimulated or rTNF stimulated cells. These studies demonstrate that rIL-1, rTNF, and rIFN-gamma have complex effects on biosynthesis and degradation which alter the quantity and molecular weight of the HA produced by lung fibroblasts. They also show that fibroblast HA degradation is mediated by a previously unrecognized lysosomal-type hyaluronidase whose function may be regulated by altering fibroblast-HA binding. Lastly, they suggest that the CD44 *HA* *receptor* may be involved in this process.

7/3,AB/103 (Item 103 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

07488194 93015928 PMID: 1383202
Identification of the Ca(2+)-independent endocytic *hyaluronan* *receptor* in rat liver sinusoidal endothelial cells using a photoaffinity cross-linking reagent.
Yannariello-Brown J; Frost S J; Weigel P H
Department of Human Biological Chemistry and Genetics, University of Texas Medical Branch, Galveston 77555-0647.
Journal of biological chemistry (UNITED STATES) Oct 5 1992, 267 (28) p20451-6, ISSN 0021-9258 Journal Code: 2985121R
Contract/Grant No.: AG05492; AG; NIA; GM35978; GM; NIGMS Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
The Ca(2+)-independent endocytic hyaluronan (*HA*) *receptor* in rat liver sinusoidal endothelial cells (LECs) was identified using a novel cross-linking derivative of HA. The heterobifunctional, photoactivatable, reducible reagent sulfosuccinimidyl 2-(p-azidosalicylamido)ethyl-1,3'-dithi opropionate (SASD) was coupled to the terminal amino group of uniquely modified HA-amine oligosaccharides (M(r) approximately 60,000) and subsequently iodinated. 125I-ASD-HA bound to cultured LECs with similar specificity and affinity as a previously characterized 125I-HA-amine/Bolton-Hunter adduct. Permeabilized LECs were incubated with 125I-ASD-HA with 10 mM EGTA and photolysed with UV light. Detergent extracts were reduced to release the HA oligosaccharides and radiolabeled proteins were analyzed by sodium dodecyl sulfate-polyacrylamide gel electrophoresis and autoradiography. Two polypeptides were consistently and equally labeled at M(r) = 175,000 and 166,000. Photoaffinity labeling of these two proteins was virtually identical in cultured LECs or membranes and was competed greater than 90% with a 100-fold excess of HA. As with the previously characterized bona fide LEC *HA* *receptor* , cross-linking was also competed by chondroitin sulfate and heparin, but less efficiently by chondroitin and not with galacturonan. We conclude that the Ca(2+)-independent LEC *HA* *receptor* is composed of at least two polypeptides of M(r) approximately 175,000 and 166,000 and may exist as a heterodimer of M(r) approximately 340,000. We also conclude that the LEC *HA* *receptor* is distinct from the CD44 family of HA-binding proteins.

7/3,AB/104 (Item 104 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

07484131 93011472 PMID: 1382996
CD44 can be activated to function as an *hyaluronic* *acid* *receptor* in normal murine T cells.
Lesley J; Hyman R
Department of Cancer Biology, Salk Institute, San Diego, CA 92186-5800. European journal of immunology (GERMANY) Oct 1992, 22 (10) p2719-23, ISSN 0014-2980 Journal Code: 1273201
Contract/Grant No.: AI-31613; AI; NIAID; CA-13287; CA; NCI; CA-14195; CA; NCI
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
The hyaluronic acid (HA)-binding function of CD44

expressed on the cell surface of normal hematopoietic cells has been studied by assaying binding of fluoresceinated hyaluronic acid (F1-HA) and adhesion to immobilized HA. As has been observed previously, normal hematopoietic cells from bone marrow and spleen do not constitutively bind HA. A CD44-specific monoclonal antibody, IRAWB 14, which has been shown to rapidly induce HA binding in some CD44+ cell lines, was used to activate the HA-binding function of CD44 in these normal cells. Only splenic T cells were activated by the IRAWB 14 antibody to bind F1-HA. Upon activation, F1-HA binding correlated with the level of CD44 expression. Activation of HA binding allowed splenic T cells to adhere to HA immobilized on plastic and to an endothelial cell line in an HA-dependent manner. BALB/c and AKR/J splenic T cells differ in their level of CD44 expression, and this correlated with differences in their ability to bind HA upon antibody activation. The minor subpopulation of MEL-14- T cells were among the brightest F1-HA-staining cells. We propose, on the basis of these and other results, that there are three states of CD44 function with respect to HA binding: (a) a non-activatable, resting state, which cannot be rapidly activated to bind HA, as seen in most hematopoietic cells; (b) an activatable state, which can be rapidly converted to HA-binding function, in this case by the IRAWB 14 antibody, illustrated by T cells as shown here; and (c) a constitutively active state, which can bind HA without antibody activation, seen in some cell lines.

7/3,AB/105 (Item 105 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

07446937 92379876 PMID: 1380898
Hyaluronan and cell locomotion.
Turley E A
Manitoba Institute of Cell Biology, Winnipeg, Canada.
Cancer and metastasis reviews (UNITED STATES) Mar 1992, 11 (1) p21-30, ISSN 0891-9992 Journal Code: 8605731
Contract/Grant No.: CA 51540 01A1; CA; NCI
Document type: Journal Article; Review; Review, Tutorial
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
Hyaluronan (HA), a glycosaminoglycan, has long been implicated in cell locomotion. We have shown that HA production regulates the locomotion of H-ras-transformed cells. This autocrine motility mechanism is mediated by a novel *HA* *receptor* termed RHAMM, an acronym for Receptor for HA Mediated Motility. HA:RHAMM interactions regulate directional locomotion of tumor cells and result in enhanced protein tyrosine phosphorylation that may be a critical messenger mechanism for initiation of locomotion.

7/3,AB/106 (Item 106 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

07415917 92348516 PMID: 1639856
Correction. Molecular cloning of a novel *hyaluronan* *receptor* that mediates tumor cell motility.
Journal of cell biology (UNITED STATES) Aug 1992, 118 (3) p753, ISSN 0021-9525 Journal Code: 0375356
Document type: Published Erratum
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed

7/3,AB/107 (Item 107 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

07366847 92299690 PMID: 1376732
Molecular cloning of a novel *hyaluronan* *receptor* that mediates tumor cell motility.
Hardwick C; Hoare K; Owens R; Hohn H P; Hook M; Moore D; Cripps V; Austen L; Nance D M; Turley E A
Department of Biochemistry, University of Alabama, Birmingham 35233. Journal of cell biology (UNITED STATES) Jun 1992, 117 (6) p1343-50, ISSN 0021-9525 Journal Code: 0375356
Contract/Grant No.: AM27807; AM; NIADDK; CA51540; CA; NCI Erratum in J Cell Biol 1992 Aug;118(3) 753
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
A cDNA encoding a unique *hyaluronan* *receptor* has been molecularly cloned from a lambda GT11 3T3 cDNA expression library. Immunoblot analyses of cell lysates, using antibodies to peptides encoded in the cDNA, specifically react with a 58-kD protein. This protein is regulated by the mutant H-ras gene in cells containing a metallothionein promoter H-ras hybrid gene. Further, antibodies to peptide sequences encoded in the cDNA block the increase in locomotion resulting from induction of the mutant H-ras gene in this cell line. In a transblot assay, the bacterially expressed protein binds to biotinylated hyaluronan. Antibodies to peptides encoded in the cDNA react in immunoblot assays with the 58- and 52-kD proteins of a novel *hyaluronan* *receptor* complex previously implicated in cell locomotion. Furthermore, antibodies specific to the 58- and 52-kD proteins, which block ras-induced locomotion, also cross-react with the expressed, encoded protein. The gene product described here appears to be a new type of *hyaluronan* *receptor* that is involved in cell locomotion. It is named RHAMM, an acronym for receptor for hyaluronan-mediated motility.

7/3,AB/108 (Item 108 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

07330547 92259539 PMID: 1374758
The endocytic *hyaluronan* *receptor* in rat liver sinusoidal endothelial cells is Ca(+2)-independent and distinct from a Ca(+2)-dependent *hyaluronan* binding activity.
Yannariello-Brown J; McGary C T; Weigel P H
Department of Human Biological Chemistry and Genetics, University of Texas Medical Branch, Galveston 77550.
Journal of cellular biochemistry (UNITED STATES) Jan 1992, 48 (1) p73-80, ISSN 0730-2312 Journal Code: 8205768
Contract/Grant No.: AG 05492; AG; NIA; GM 35978; GM; NIGMS Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
Isolated and cultured rat liver sinusoidal endothelial cells (LECs) retain the ability to specifically bind 125I-hyaluronan (HA) and internalize it using a coated pit pathway [Biochem J, 257:875-884, 1989]. Here we have determined the effect of Ca+2 on the binding and endocytosis of HA by LECs. 125I-HA binding to intact LECs at 4 degrees C occurred both in the absence (10 mM EGTA) or the presence of physiologic concentrations of Ca+2 (1.8 mM). However, the specific binding of 125I-HA to LECs increased linearly with increasing Ca+2 concentrations. After permeabilization with the nonionic detergent digitonin, the Ca(+2)-independent HA binding activity increased approximately 743%, while the Ca(+2)-dependent binding activity was enhanced only approximately 46%. Therefore, the Ca(+2)-dependent HA binding activity appears not to be intracellular, whereas the Ca(+2)-independent *HA* *receptor* is found both inside LECs and on the cell surface. When LECs were allowed to endocytose 125I-HA at 37 degrees C in 10 mM EGTA or in 1.8 mM Ca+2, no differences were seen in the extent or rate of endocytosis. When LECs were allowed to endocytose 125I-HA in the presence of 10 mM Ca+2, the amount of cell-associated radioactivity increased approximately 20-50-fold. However, this additional cell-associated 125I-HA was not sensitive to hyperosmolarity and was removed by washing the cells in 10 mM EGTA at 4 degrees C. Therefore, the Ca(+2)-dependent cell-associated 125I-HA had accumulated on the cell surface and had not been internalized. From these studies we conclude that LECs have at least two types of specific HA binding sites.(ABSTRACT TRUNCATED AT 250 WORDS)

7/3,AB/109 (Item 109 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

07328759 92256965 PMID: 1374658
The role of *hyaluronan*-binding protein in assembly of pericellular matrices.
Yu Q; Banerjee S D; Toole B P
Department of Anatomy and Cellular Biology, Tufts University Health Science Schools, Boston, Massachusetts 02111.
Developmental dynamics : an official publication of the American Association of Anatomists (UNITED STATES) Feb 1992, 193 (2) p145-51, ISSN 1058-8388 Journal Code: 9201927
Contract/Grant No.: DE05838; DE; NIDCR; P01 HD23681; HD; NICHD Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
Hyaluronan-dependent pericellular matrices or "coats" are expressed by a variety of cell types in culture and modulation of their expression may be important in regulation of cell interactions in vivo during development. Monoclonal antibody IVd4, which recognizes hyaluronan-binding protein with the properties of a *hyaluronan* *receptor*, was shown to block formation of these coats by a variety of cells. Using rat fibrosarcoma cells, it was found that the antibody not only blocked initial formation of the coats but also caused their loss when added subsequent to formation. The loss of preformed coats in the presence of antibody occurred at 4 degrees and 37 degrees, implying that the function of hyaluronan-binding protein in coat formation is not in mediating metabolic processes. The antibody also had no significant effect on hyaluronan production by the fibrosarcoma cells. In addition, hyaluronan hexasaccharide, a competitive inhibitor of the interaction between polymeric hyaluronan and its cell surface receptor, was found to inhibit coat formation. Thus it is concluded that a hyaluronan-binding protein with the properties of a *hyaluronan* *receptor* is required for pericellular matrix formation.

7/3,AB/110 (Item 110 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

07298369 92225276 PMID: 1563592
Hyaluronan.
Laurent T C; Fraser J R
Department of Medical and Physiological Chemistry, University of Uppsala, Sweden.
FASEB journal : official publication of the Federation of American Societies for Experimental Biology (UNITED STATES) Apr 1992, 6 (7) p2397-404, ISSN 0892-6638 Journal Code: 8804484

Document type: Journal Article; Review; Review, Tutorial
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed

Hyaluronan (hyaluronic acid) is a high-molecular-mass polysaccharide found in the extracellular matrix, especially of soft connective tissues. It is synthesized in the plasma membrane of fibroblasts and other cells by addition of sugars to the reducing end of the polymer, whereas the nonreducing end protrudes into the pericellular space. The polysaccharide is catabolized locally or carried by lymph to lymph nodes or the general circulation, from where it is cleared by the endothelial cells of the liver sinusoids. The overall turnover rate is surprisingly rapid for a connective tissue matrix component (t1/2 0.5 to a few days). Hyaluronan has been assigned various physiological functions in the intercellular matrix, e.g., in water and plasma protein homeostasis. Hyaluronan production increases in proliferating cells and the polymer may play a role in mitosis. Extensive hyaluronidase-sensitive coats have been identified around mesenchymal cells. They are either anchored firmly in the plasma membrane or bound via hyaluronan-specific binding proteins (receptors). Such receptors have now been identified on many different cells, e.g., the lymphocyte homing receptor CD 44. Interaction between a *hyaluronan* *receptor* and extracellular polysaccharide has been connected with locomotion and cell migration. Hyaluronan seems to play an important role during development and differentiation and has other cell regulatory activities. Hyaluronan has also been recognized in clinical medicine. A concentrated solution of hyaluronan (10 mg/ml) has, through its tissue protective and rheological properties, become a device in ophthalmic surgery. Analysis of serum hyaluronan is promising in the diagnosis of liver disease and various inflammatory conditions, e.g., rheumatoid arthritis. Interstitial edema caused by accumulation of hyaluronan may cause dysfunction in various organs.

7/3,AB/111 (Item 111 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

07198284 92129427 PMID: 1370836

The *hyaluronan* *receptor* (CD44) participates in the uptake and degradation of *hyaluronan*.

Culty M; Nguyen H A; Underhill C B
Department of Anatomy and Cell Biology, Georgetown Medical Center, Washington, DC 20007.

Journal of cell biology (UNITED STATES) Feb 1992, 116 (4) p1055-62, ISSN 0021-9525 Journal Code: 0375356
Contract/Grant No.: HD26758; HD; NICHD; HL41565; HL; NHLBI Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed

The *hyaluronan* *receptor* belongs to the polymorphic family of CD44 glycoproteins, which have been implicated in a variety of cellular functions including adhesion to hyaluronan and collagen, the binding of lymphocytes to high endothelial cells during extravasation, and conferring metastatic potential to carcinoma cells. Here, we demonstrate that the receptor also participates in the uptake and degradation of hyaluronan by both transformed fibroblasts (SV-3T3 cells) and alveolar macrophages. These cells were incubated with isotopically labeled hyaluronan for various periods of time, and the extent of degradation was determined by either molecular-sieve chromatography or centrifugation through Centricon 30 microconcentrators. The macrophages degraded the hyaluronan at a faster rate than the SV-3T3 cells, which may reflect the fact that they contained a greater number of receptors. More importantly, in both cell types, the degradation of hyaluronan was specifically blocked by antibodies directed against the receptor. However, the receptor by itself did not have the ability to degrade hyaluronan, since preparations of SV-3T3 membranes containing the receptor did not break down hyaluronan. Subsequent experiments revealed that macrophages can internalize fluorescein-tagged hyaluronan, and this process was blocked by antibodies against the receptor. Furthermore, the subsequent degradation of hyaluronan was inhibited by agents that block the acidification of lysosomes (chloroquine and NH4Cl). Thus, the most likely explanation for these results is that the receptor mediates the uptake of hyaluronan into the cell where it can be degraded by acid hydrolases in lysosomes. The ability of cells expressing the receptor to degrade hyaluronan may be important during tissue morphogenesis and cell migration.

7/3,AB/112 (Item 112 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

07195522 92118858 PMID: 1370630

Detergent solubilization of the endocytic Ca(2+)-independent *hyaluronan* *receptor* from rat liver endothelial cells and separation from a Ca(2+)-dependent *hyaluronan*-binding activity.

Yannariello-Brown J; Weigel P H
Department of Human Biological Chemistry and Genetics, University of Texas Medical Branch, Galveston 77550.

Biochemistry (UNITED STATES) Jan 21 1992, 31 (2) p576-84, ISSN 0006-2960 Journal Code: 0370623
Contract/Grant No.: AG 05492; AG; NIA; GM 35978;

GM; NIGMS Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
Rat liver sinusoidal endothelial cells (LECs) mediate the removal of hyaluronan (HA) from the circulation via a specific Ca(2+)-independent endocytic receptor. To characterize the receptor biochemically, detergent-soluble extracts were prepared from crude LEC membranes. Using a dot blot assay to quantitate 125I-HA binding activity in CHAPS-solubilized membranes, we detected not only specific Ca(2+)-independent but also specific Ca(2+)-dependent HA-binding activity. Both HA-binding activities behave as integral membrane-associated proteins; they are not released from LEC membranes by treatment at pH 11, and they require detergent for extraction. The Ca(2+)-independent *HA* *receptor* was inactivated by treatment at 56 degrees C for 30 min or with 200 mM DTT at 4 degrees C for 30 min, whereas the Ca(2+)-dependent activity actually increased by 75% after treatment at 56 degrees C and only 20% of the Ca(2+)-dependent activity was lost after DTT treatment. A two-cycle membrane extraction protocol using CHAPS partially separated the two HA-binding activities. Eight millimolar KCl and 0.5% CHAPS extracted approximately 50% of the Ca(2+)-independent *HA* *receptor* , but only 4-11% of the Ca(2+)-dependent activity. When the KCl and CHAPS concentrations were increased to 2.0 M and 1.5%, respectively, the remaining *HA* *receptor* , as well as 89-96% of the Ca(2+)-dependent activity, was then extracted. The Ca(2+)-independent and Ca(2+)-dependent activities could also be further separated using Sephacryl S-400 gel filtration chromatography.(ABSTRACT TRUNCATED AT 250 WORDS)

7/3,AB/113 (Item 113 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

07044833 91358568 PMID: 1715873
Assembly of a chondrocyte-like pericellular matrix on non-chondrogenic cells. Role of the cell surface *hyaluronan* receptors in the assembly of a pericellular matrix.
Knudson W; Knudson C B
Department of Biochemistry, Rush-Presbyterian-St Luke's Medical Center, Chicago, Illinois 60612.
Journal of cell science (ENGLAND) Jun 1991, 99 (Pt 2) p227-35, ISSN 0021-9533 Journal Code: 0052457
Contract/Grant No.: AR-39239; AR; NIAMS
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
In this study, we have examined the capacity of various cell types, which express cell surface hyaluronan receptors, to organize a chondrocyte-like pericellular matrix when given chondrocyte-derived extracellular matrix macromolecules exogenously. The assembly of a pericellular matrix was visualized by a particle exclusion assay. Without the addition of exogenous macromolecular components, none of the cell types studied exhibited significant pericellular matrices extending from their plasma membranes. However, upon the addition of high molecular weight hyaluronan in combination with aggregating cartilage proteoglycan monomers, large pericellular matrices were formed within two hours of incubation. No pericellular matrices were formed if these macromolecular components were added separately at equivalent concentrations or if the components were added in the presence of hyaluronan hexasaccharide, a competitive inhibitor of hyaluronan interaction with cell surface hyaluronan receptors. Fully assembled pericellular matrices could also be displaced by the subsequent addition of hyaluronan hexasaccharides. Nonliving, glutaraldehyde-fixed cells, which retained functional hyaluronan receptors, maintained the capacity to assembly pericellular matrices with exogenous components, in serum-containing or serum-free medium. Cells that were incubated with exogenous matrix macromolecules for 24 h, followed by a chase incubation in medium minus the exogenous macromolecules, continued to maintain the matrix for up to 6 h on live cells and more than 24 h on glutaraldehyde-fixed cells. Cell types that did not express hyaluronan receptors were not capable of organizing such pericellular matrices when incubated with these exogenous components. These findings suggest that cells expressing hyaluronan receptors have a significant capacity to organize their immediate extracellular environment via hyaluronan-*hyaluronan* *receptor* interactions. Possible physiological functions for this type of matrix organizing capacity are discussed.

7/3,AB/114 (Item 114 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

06974504 91285236 PMID: 1711984
Monoclonal antibody to chick embryo *hyaluronan*-binding protein: changes in distribution of binding protein during early brain development. Banerjee S D; Toole B P
Department of Anatomy and Cellular Biology, Tufts University Health Science Schools, Boston, Massachusetts 02111.
Developmental biology (UNITED STATES) Jul 1991, 146 (1) p186-97, ISSN 0012-1606 Journal Code: 0372762

Contract/Grant No.: DE05838; DE; NIDCR; HD23681; HD; NICHD Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
A monoclonal antibody, MAb IVd4, that recognizes hyaluronan-binding protein (HABP) from chick embryo brain has been produced and characterized. By immunoblotting, MAb IVd4 was shown to recognize three proteins in chick embryo brain of molecular weight 93, 90, and 69 kDa; this interaction was inhibited by addition of hyaluronan hexasaccharides. Overlay of transblots with [3H]hyaluronan showed binding to proteins of similar molecular weight. MAb IVd4 blocked binding of [3H]hyaluronan to brain HABP and to simian virus-transformed 3T3 cells, indicating a possible relationship with the 85-kDa *hyaluronan* *receptor* of these cells. The distribution of HABP during early brain development was analyzed by immunohistochemistry. Immunoreactivity was uniform in newly formed neuroectoderm but became more concentrated in the roof of the brain during the second day of embryonic development. As the neuroectoderm becomes layered, the HABP was increasingly restricted to the forming plexiform layer, an area enriched in neural cell processes. Immunoreactivity was greatly enhanced by pretreatment of tissue with hyaluronidase, presumably due to removal of hyaluronan bound to the HABP, and was abolished on treatment with hyaluronan hexasaccharide, presumably due to inhibition of HABP-antibody interaction. These results suggest that a *hyaluronan* *receptor* is involved in early cellular events in brain development.

7/3,AB/115 (Item 115 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

06953346 91265530 PMID: 1710929
Characterization and purification of the *hyaluronan*-*receptor* on liver endothelial cells.
Forsberg N; Gustafson S
Department of Medical and Physiological Chemistry, University of Uppsala, Sweden.
Biochimica et biophysica acta (NETHERLANDS) May 30 1991, 1078 (1) p12-8, ISSN 0006-3002 Journal Code: 0217513
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
In order to characterize the proteins on liver endothelial cells that bind hyaluronan (HYA), liver endothelial cells were surface-iodinated with 125I, solubilized by Triton X-100 and passed through a column containing HYA coupled to agarose. The column was washed and eluted with HYA-oligosaccharides. Sodium dodecyl sulfate polyacrylamide gel electrophoresis (SDS-PAGE) of the eluted material, followed by autoradiography, showed a major band with a molecular mass of 100 kDa, that upon reduction gave major bands of 20 and 35 kDa, and minor doublet bands at 60 and 80 kDa. Two-dimensional electrophoresis of liver endothelial cell membrane proteins revealed that the 100 kDa protein has a pI of 6.6-6.8. The protein was purified by preparative SDS-PAGE of liver endothelial cell membrane proteins. The 100 kDa protein was excised from the gel and used for immunization of rabbits. Antiserum from immunized rabbits specifically recognized only the 100 kDa protein on immunoblots of liver endothelial cell membrane proteins separated by SDS-PAGE. The binding of 3H-HYA to liver endothelial cells and liver endothelial cell membranes could be specifically inhibited by Fab-fragments of the antibodies. When we tried to isolate the receptor in large scale by affinity chromatography of proteins from purified liver endothelial cell membranes, the 100 kDa protein could often not be detected on immunoblots or by silver staining following SDS-PAGE of the eluted material. Instead, proteins with molecular masses of 55 and 15 kDa were detected, but the antibodies reacted specifically with these proteins. Thus the 100 kDa protein is apparently susceptible to cleavage into distinct subcomponents.

7/3,AB/116 (Item 116 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

06497294 90201279 PMID: 2180732
Binding of *hyaluronic* acid to lymphoid cell lines is inhibited by monoclonal antibodies against Pgp-1.
Lesley J; Schulte R; Hyman R
Salk Institute, San Diego, California 92138.
Experimental cell research (UNITED STATES) Apr 1990, 187 (2) p224-33 , ISSN 0014-4827 Journal Code: 0373226
Contract/Grant No.: CA 25893; CA; NCI
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
Recent biochemical and sequence data suggest a possible relationship between Pgp-1 (identical to CD44/Hermes 1/p85) and a hyaluronic acid-binding function. Here, we have studied the hyaluronic acid-binding activity of a series of murine hematopoietic cell lines using several assays: cell aggregation by hyaluronic acid, binding of fluorescein-conjugated hyaluronic acid, and cell adhesion to hyaluronic acid-coated dishes. Certain Pgp-1-positive T and B cell lines show hyaluronic acid binding that is highly specific and is not competed for by

other glycosaminoglycans. Monoclonal antibodies against Pgp-1, but not antibodies against other major cell surface glycoproteins, inhibited hyaluronic acid-induced cell aggregation and cell adhesion to hyaluronic acid-coated dishes. Additionally, some anti-Pgp-1 antibodies inhibited binding of fluorescein-hyaluronic acid to hyaluronic acid-binding lines. We found no Pgp-1-negative lines that bound, but many Pgp-1-positive cell lines did not bind hyaluronic acid. Two Pgp-1-positive thymomas that did not bind hyaluronic acid were induced by phorbol ester to bind hyaluronic acid with the same specificity as other hyaluronic acid-binding lines. Normal hematopoietic cells, including those which express high levels of Pgp-1, such as bone marrow myeloid cells and splenic lymphocytes, showed no detectable hyaluronic acid-binding activity. We discuss several models that might account for these observations: (1) the *hyaluronic* *acid* *receptor* is Pgp-1, but it normally exists in an inactive state; (2) hyaluronic acid receptors are a subset of a family of molecules recognized by anti-Pgp-1 antibodies; (3) the *hyaluronic* *acid* *receptor* is not Pgp-1, but is closely associated with Pgp-1 on the surface of cells which express hyaluronic acid-binding activity.

7/3,AB/117 (Item 117 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

06338470 90032068 PMID: 2680346
The specific interaction between fibrin(ogen) and *hyaluronan*: possible consequences in haemostasis, inflammation and wound healing. Weigel P H; Frost S J; LeBoeuf R D; McGary C T
Department of Human Biological Chemistry and Genetics, University of Texas Medical Branch, Galveston 77550.
Ciba Foundation symposium (NETHERLANDS) 1989, 143 p248-61; discussion 261-4, 281-5, ISSN 0300-5208 Journal Code: 0356636
Contract/Grant No.: GM 35978; GM; NIGMS
Document type: Journal Article; Review; Review, Tutorial
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
We have proposed that fibrin and hyaluronan (HA) are macromolecular regulators during inflammation and wound healing. Here we extend our studies to characterize the specific interaction between fibrin(ogen) and HA. 125I-labelled HA (Mr approximately 32,000) was bound by plastic surfaces coated with human fibrinogen but not bovine serum albumin, ovalbumin, beta-lactoglobin or rabbit immunoglobulin G. 125I-labelled fibrinogen bound to a unique hexylamine derivative of HA coupled to Sepharose and was eluted specifically by HA oligosaccharides in a size-dependent manner. A dot blot assay, in which proteins are adsorbed to nitrocellulose and probed with 125I-HA, also showed specific binding to human fibrinogen. This assay was used to examine fibrinogens from other mammalian species. No specific 125I-HA binding was observed with the protein from horse, rat or cow. Significant binding was detected with human, sheep, rabbit, dog, baboon, goat and pig fibrinogens. Thrombin-induced formation of fibrin clots is also affected by HA, which decreases the lag time before clotting and increases the rate of clot formation. The rate of fibrin polymerization increased over 500% in the presence of 60 microM HA. Furthermore, the structure of the fibrin gel, as assessed by light scattering, was altered by HA or chondroitin sulphate in a concentration-dependent manner. The results support the proposed wound-healing model and indicate that an increase in circulating HA levels could adversely affect haemostasis and increase the risk of thrombosis or bleeding. The interaction between HA and fibrinogen emphasizes the importance of the liver endothelial cell *HA* *receptor* in the removal of glycosaminoglycans from the blood. Cultured cells continuously endocytosing 125I-HA for 4 h reutilized their total cellular HA receptors at least once every 50 min even in the presence of cycloheximide. This endocytotic receptor was therefore shown to be part of a recycling system.

7/3,AB/118 (Item 118 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

06111497 89193499 PMID: 2930491
Endocytosis of *hyaluronic* acid by rat liver endothelial cells. Evidence for receptor recycling.
McGary C T; Raja R H; Weigel P H
Department of Human Biological Chemistry and Genetics, University of Texas Medical Branch, Galveston 77550.
Biochemical journal (ENGLAND) Feb 1 1989, 257 (3) p875-84, ISSN 0264-6021 Journal Code: 2984726R
Contract/Grant No.: GM 35978; GM; NIGMS
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
Hyaluronic acid (HA) is cleared from the blood by liver endothelial cells through receptor-mediated endocytosis [Eriksson, Fraser, Laurent, Pertoft & Smedsrod (1983) Exp. Cell Res. 144, 223-238]. We have measured the capacity of cultured rat liver endothelial cells to endocytose and degrade 125I-HA (Mr approximately 44,000) at 37 degrees C. Endocytosis was linear for 3 h and then reached a plateau. The rate of endocytosis was concentration-dependent and reached a maximum of 250 molecules/s per cell. Endocytosis of

125I-HA was inhibited more than 92% by a 150-fold excess of non-radiolabelled HA. HA, chondroitin sulphate and heparin effectively competed for endocytosis of 125I-HA, whereas glucuronic acid, N-acetylglucosamine, DNA, RNA, polygalacturonic acid and dextran did not compete. In the absence of cycloheximide, endothelial cells processed 13 times more 125I-HA in 6 h than their total (cell-surface and intracellular) specific HA-binding capacity. This result was not due to degradation and rapid replacement of receptors, because, even in the presence of cycloheximide, these cells processed 6 times more HA than their total receptor content in 6 h. Also, in the presence of cycloheximide, no decrease in 125I-HA-binding capacity was seen in cells processing or not processing HA for 6 h, indicating that receptors are not degraded after the endocytosis of HA. During endocytosis of HA at 37 degrees C, at least 65% of the intracellular HA receptors became occupied with HA within 30 min. This indicates that the intracellular HA receptors (75% of the total) function during continuous endocytosis. Hyperosmolarity inhibits endocytosis and receptor recycling in the asialoglycoprotein and low-density-lipoprotein receptor systems by disrupting the coated-pit pathway [Heuser & Anderson (1987) J. Cell Biol. 105, 230a; Oka & Weigel (1988) J. Cell. Biochem. 36, 169-183]. Hyperosmolarity inhibited 125I-HA endocytosis in liver endothelial cells by more than 90%, suggesting use of a coated-pit pathway by this *HA* *receptor*. We conclude that liver endothelial cell HA receptors are recycled during the continuous endocytosis and processing of HA.

7/3,AB/119 (Item 119 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

05949526 89034151 PMID: 2460454
Affinity and distribution of surface and intracellular *hyaluronic* acid receptors in isolated rat liver endothelial cells.
Raja R H; McGary C T; Weigel P H
Department of Human Biological Chemistry and Genetics, University of Texas Medical Branch, Galveston 77550.
Journal of biological chemistry (UNITED STATES) Nov 15 1988, 263 (32) p16661-8, ISSN 0021-9258 Journal Code: 2985121R
Contract/Grant No.: GM35978; GM; NIGMS
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
125I-Hyaluronic acid (HA) uniquely modified only at the reducing end (Raja, R.H., LeBoeuf, R. D., Stone, G.W., and Weigel, P.H. (1984) Anal. Biochem. 139, 168-177) binds specifically to rat liver endothelial cells in suspension or in culture. About 67-85% of the HA binding sites in isolated cells in suspension and 50% in cultured cells were intracellular, since they were exposed after permeabilizing cells with digitonin. Specific 125I-HA binding at 4 degrees C varied from 60 to 80% for intact cells and from 70 to 90% for permeabilized cells. Freshly isolated permeabilized cells bound about 500,000 HA molecules/cell at saturation. Within 5 h of culture, however, total HA binding decreased to 250,000 molecules/cells and then remained constant for at least 36 h. Surface *HA* *receptor* activity was essentially the same on cultured cells or cells in suspension (approximately 10(5)/cell). Cultured cells had 1.8 x 10(5) fewer intracellular receptors/cell. The affinities of surface and intracellular receptors of cells in culture and in suspension were essentially the same. The average Kd, determined by equilibrium binding studies, was 5.8 +/- 2.8 x 10(-8) M (n = 12). Dissociation of bound 125I-HA from permeable cultured cells was rapid (t1/2 = 30.9 min;kappa off = 3.7 x 10(-4) s-1). A variety of carbohydrates had essentially identical effects on 125I-HA binding to surface or total cellular receptors in cells in culture or in suspension. Chondroitin sulfate and heparin competed almost as effectively as unlabeled HA for 125I-HA binding at 4 degrees C. Other saccharides including polygalacturonic acid, dextran, glucuronic acid, and N-acetylglucosamine competed poorly or not at all. We conclude that (i) the 125I-HA binding sites within liver endothelial cells are HA receptors, identical in affinity and specificity to those on the cell surface; (ii) the distribution of cellular HA receptors is similar to other receptor systems with about 50-80% being intracellular; (iii) the liver endothelial cell *HA* *receptor* recognizes several glycosaminoglycans; and (iv) the liver endothelial receptor is different in function and characteristics than the fibroblast *HA* *receptor*.

7/3,AB/120 (Item 1 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci

09365475 Genuine Article#: 377QY Number of References: 0 Title: Regulation of the *hyaluronan* *receptor* CD44 by phosphorylation and cytoskeletal association
Author(s): Legg JW; Lewis CA; Isacke CM
Corporate Source: Univ London Imperial Coll Sci Technol & Med,London SW7 2AZ//England/
Journal: MOLECULAR BIOLOGY OF THE CELL, 2000, V11, S (DEC), P477A-477A ISSN: 1059-1524 Publication date: 20001200
Publisher: AMER SOC CELL BIOLOGY, 8120 WOODMONT AVE, STE 750, BETHESDA, MD

20814-2755 USA
Language: English Document Type: MEETING ABSTRACT

7/3,AB/121 (Item 2 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci
(c) 2002 Inst for Sci Info. All rts. reserv.

09363551 Genuine Article#: 377QY Number of References: 0 Title: Localization of HARE - The *hyaluronan* *receptor* for endocytosis.
Author(s): McGary CT; Zhou B; Duff B; Weigel PH; Weigel PH Corporate Source: Univ Rochester,Med Ctr,Rochester//NY/14642; Univ Oklahoma,Hlth Sci Ctr,Oklahoma City//OK/73190
Journal: MOLECULAR BIOLOGY OF THE CELL, 2000, V11, S (DEC), P105A-106A ISSN: 1059-1524 Publication date: 20001200
Publisher: AMER SOC CELL BIOLOGY, 8120 WOODMONT AVE, STE 750, BETHESDA, MD 20814-2755 USA
Language: English Document Type: MEETING ABSTRACT

7/3,AB/122 (Item 3 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci
(c) 2002 Inst for Sci Info. All rts. reserv.

09160452 Genuine Article#: 360JN Number of References: 0 Title: Characterization of the *hyaluronan* *receptor* for endocytosis (HARE).
Author(s): Weigel PH; Zhou B; Weigel JA; McGary CT Corporate Source: UNIV OKLAHOMA,HLTH SCI CTR, DEPT BIOCHEM & MOL BIOL/OKLAHOMA CITY//OK/73190; UNIV ROCHESTER,SCH MED, DEPT PATHOL/ROCHESTER//NY/14642
Journal: GLYCOBIOLOGY, 2000, V10, N10 (OCT), P31-31 ISSN: 0959-6658 Publication date: 20001000
Publisher: OXFORD UNIV PRESS INC, JOURNALS DEPT, 2001 EVANS RD, CARY, NC 27513
Language: English Document Type: MEETING ABSTRACT

7/3,AB/123 (Item 4 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci
(c) 2002 Inst for Sci Info. All rts. reserv.

09070437 Genuine Article#: 363FW Number of References: 46 Title: Expression of *hyaluronan* receptors CD44 and RHAMM in stomach cancers: relevance with tumor progression (ABSTRACT AVAILABLE) Author(s): Li H (REPRINT) ; Guo L; Li JW; Liu N; Qi R; Liu J Corporate Source: SHENYANG MED COLL,DIV MOL BIOL/SHENYANG 110031//PEOPLES R CHINA/ (REPRINT)
Journal: INTERNATIONAL JOURNAL OF ONCOLOGY, 2000, V17, N5 (NOV), P927-932 ISSN: 1019-6439
Publication date: 20001100
Publisher: PROFESSOR D A SPANDIDOS, 1, S MERKOURI ST, EDITORIAL OFFICE, ATHENS 116 35, GREECE
Language: English Document Type: ARTICLE
Abstract: Interactions of hyaluronic acid (HA) with its binding proteins CD44 and RHAMM (receptor for HA-mediating motility) have been proposed to be important in promoting tumor progression and dissemination. However, a comparative study of their expression patterns in stomach cancer and its associated lesions is not yet available. To address this issue, the combined examinations of pathology, immunocytochemistry and Western blot hybridization were performed on advanced gastric cancer specimens as well as their preneoplastic and non-cancerous counterparts. Alternative CD44 expression was observed in the gastric mucosa with different lesions. CD44 proteins harboring variant exon 6 (CD44 v6) was detected only in cancer tissues with a total positive rate of 14% (10/74). Intracellular RHAMM molecules in Mr 93000 to 95000 were expressed in 3/31 non-cancerous mucosa. RHAMM detection rates increased along with tumor progression. Irrespective of the differences of gross and morphological pattern, majority (54/74) of cancer cases expressed multiple RHAMM isoforms in Mr 40000-45000, 64000, 70000-73000, 85000 and 93000-95000 with the appearance of cell surface immunocytochemical labeling. Among CD44 variant isoforms, v6 is more relevant with malignant transformation of gastric epithelium. Expression of RHAMM, especially the cell surface variants, is closely correlated with tumor progression ($P<0.01$). Expression of CD44 and RHAMM may benefit the invasion and metastasis of gastric cancer cells presumably in a reciprocal manner.

7/3,AB/124 (Item 5 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci
(c) 2002 Inst for Sci Info. All rts. reserv.

08259327 Genuine Article#: 260JL Number of References: 0 Title: Monoclonal antibody antagonists of RHAMM, a *hyaluronan* *receptor* that is highly expressed in human tumor cell lines, and required for activation of MAP kinase.
Author(s): Jackson JR; Gilmartin A; Abrahamson J; Holmes SD; Ho ML; Matico R; Fornwald J; Winkler JD Corporate Source: SMITHKLINE BEECHAM PHARMACEUT,/KING OF PRUSSIA//PA/19406 Journal: CLINICAL CANCER RESEARCH, 1999, V5, S (NOV),

P209-209 ISSN: 1078-0432 Publication date: 19991100
Publisher: AMER ASSOC CANCER RESEARCH, PO BOX 11806, BIRMINGHAM, AL 35202 Language: English
Document Type: MEETING ABSTRACT

7/3,AB/125 (Item 6 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci
(c) 2002 Inst for Sci Info. All rts. reserv.

08156922 Genuine Article#: 230DT Number of References: 0 Title: *Hyaluronan* *receptor* regulation of endothelial cell migration, proliferation and tube formation.
Author(s): DeLisser HM; Zhou Z; Savani RC
Corporate Source: UNIV PENN,SCH MED, DEPT MED/PHILADELPHIA//PA/19104; UNIV PENN,SCH MED, DEPT PEDIAT/PHILADELPHIA//PA/19104
Journal: AMERICAN JOURNAL OF RESPIRATORY AND CRITICAL CARE MEDICINE, 1999 , V159, N3,S (MAR), PA746-A746
ISSN: 1073-449X Publication date: 19990300
Publisher: AMER LUNG ASSOC, 1740 BROADWAY, NEW YORK, NY 10019 Language: English Document Type: MEETING ABSTRACT

7/3,AB/126 (Item 7 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci
(c) 2002 Inst for Sci Info. All rts. reserv.

08110465 Genuine Article#: 240DF Number of References: 0 Title: Purification and characterization of the endocytic *hyaluronan* *receptor* from rat liver sinusoidal endothelial cells Author(s): Zhou B; Oka JA; Singh A; Weigel PH
Corporate Source: UNIV OKLAHOMA,HLTH SCI CTR, DEPT BIOCHEM & MOL BIOL/OKLAHOMA CITY//OK/73190
Journal: GLYCOBIOLOGY, 1999, V9, N10 (OCT), P164-164
ISSN: 0959-6658 Publication date: 19991000
Publisher: OXFORD UNIV PRESS, GREAT CLARENDON ST, OXFORD OX2 6DP, ENGLAND Language: English
Document Type: MEETING ABSTRACT

7/3,AB/127 (Item 8 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci
(c) 2002 Inst for Sci Info. All rts. reserv.

08101971 Genuine Article#: 226QW Number of References: 0 Title: Mediation of *hyaluronic* acid functions and signaling in endothelial cells by an *HA* *receptor* RHAMM
Author(s): Lokeshwar VB; Seizer MG
Corporate Source: UNIV MIAMI,SCH MED/MIAMI//FL/
Journal: FASEB JOURNAL, 1999, V13, N4,1,S (MAR 12), PA45-A45 ISSN: 0892-6638 Publication date: 19990312
Publisher: FEDERATION AMER SOC EXP BIOL, 9650 ROCKVILLE PIKE, BETHESDA, MD 20814-3998
Language: English Document Type: MEETING ABSTRACT

7/3,AB/128 (Item 9 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci
(c) 2002 Inst for Sci Info. All rts. reserv.

08076362 Genuine Article#: 228JG Number of References: 0 Title: Cellular redistribution of the *hyaluronan* (*HA*) *receptor* rhamm is regulated by *HA* binding. Author(s): Gares S; Crainie M; Pilarski L
Corporate Source: UNIV ALBERTA,/EDMONTON/AB T6G 1Z2/CANADA/ Journal: FASEB JOURNAL, 1999, V13, N5,2,S (MAR 15), PA1134-A1134 ISSN: 0892-6638
Publication date: 19990315
Publisher: FEDERATION AMER SOC EXP BIOL, 9650 ROCKVILLE PIKE, BETHESDA, MD 20814-3998
Language: English Document Type: MEETING ABSTRACT

7/3,AB/129 (Item 10 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci
(c) 2002 Inst for Sci Info. All rts. reserv.

07582001 Genuine Article#: 184GE Number of References: 5 Title: Expression pattern of *hyaluronan* and fibronectin receptors in human granulation tissue (ABSTRACT AVAILABLE)
Author(s): Koschnick M (REPRINT) ; Busser F; Rosken F; Hanselmann R; Koch B ; Menger MD; Mutschler W
Corporate Source: BG UNFALLKLIN,ABT VERBRENNUNGEN PLAST & HANDCHIRURG/D-67071 LUDWIGSHAFEN//GERMANY/ (REPRINT); UNIV SAARLANDES KLINIKEN,ABT UNFALL HAND & WIEDERHERSTELLUNGSCHIRURG/HOMBURG//GERMANY/; UNIV SAARLAND,INST KLIN EXPT CHIRURG/HOMBURG//GERMANY/; UNIV SAARLANDES KLINIKEN,MED KLIN/HOMBURG//GERMANY/; UNIV SAARLANDES KLINIKEN,POLIKLIN INNERE MED 1/HOMBURG//GERMANY/; RHEIN WESTFAL TH AACHEN,KLIN PLAST CHIRURG HAND & VERBRENNUNGSCHIRURG/AACHEN//GERMANY/
Journal: LANGENBECKS ARCHIVES OF SURGERY, 1999, 1, P133-136 ISSN: 1435-2443 Publication date: 19990000
Publisher: SPRINGER VERLAG, 175 FIFTH AVE, NEW YORK, NY 10010 Language: German Document Type: ARTICLE

Abstract: Aim: Fibronectin and hyaluronan (HA) are involved in proliferation and migration of cells fron the adjacent tissue into the provisional granulation tissue matrix in wound healing. Therefore the aim of our study was to compare the expression pattern of the fibronectin and HA-receptors on fibroblasts in regular healing and chronic wounds.

Methods: Biopsies from patients with regular open wound healing (n = 10) and chronic wounds (n = 10) were taken. A single cell suspension was double labeled with monoclonal antibodies and investigated by FACS-Analysis (Fibroblasts: FITC-labeled, alpha4 and alpha5 subunits of fibronectin receptors, GD44-*HA*-*receptor*: PE-labeled). The results include the percentage of positive fibroblasts and the mean fluorescence intensity.

Results: Granulation tissue of normal and chronic human wounds showed a similar high distribution pattern of the *HA*- *receptor* CD44 on fibroblasts. The alpha4 and alpha5 subunits of fibronectin receptors were significant increased in chronic wounds by their n umber of positive cells and mean fluorescence intensity.

Conclusion: The high levels of CD44 positive fibroblasts explain the improved wound healing by HA in regular and chronic wounds. An altered matrix due to the increased presence of proteases in chronic wounds and the resulting digestion of the fibronectin matrix could explain the high expression of fibronectin receptors.

7/3,AB/130 (Item 11 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci
(c) 2002 Inst for Sci Info. All rts. reserv.

07371196 Genuine Article#: 154AM Number of References: 0 Title: The *hyaluronic* *acid* *receptor* (CD44) is expressed in bovine oocytes and preimplantational stage embryos
Author(s): Valcarcel A; deMatos DG; Furnus CC
Corporate Source: CTR INVEST REPROD PEREZ COMPANC,/RA-1084 BUENOS AIRES/DF/ARGENTINA/
Journal: THERIOGENOLOGY, 1999, V51, N1 (JAN 1), P193-193
ISSN: 0093-691X Publication date: 19990101
Publisher: ELSEVIER SCIENCE INC, 655 AVENUE OF THE AMERICAS, NEW YORK, NY 10010
Language: English Document Type: MEETING ABSTRACT

7/3,AB/131 (Item 12 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci
(c) 2002 Inst for Sci Info. All rts. reserv.

07297466 Genuine Article#: 141AW Number of References: 0 Title: HAR: A novel homolog of CD44 and putative *hyaluronic* *acid* *receptor* encoded by a gene on human chromosome 11p15. Author(s): Winkelmann JC; Basu S
Corporate Source: UNIV CINCINNATI,SCH MED/CINCINNATI//OH/
Journal: BLOOD, 1998, V92, N10,1,1 (NOV 15), P2415-2415
ISSN: 0006-4971 Publication date: 19981115
Publisher: W B SAUNDERS CO, INDEPENDENCE SQUARE WEST CURTIS CENTER, STE 300, PHILADELPHIA, PA 19106-3399
Language: English Document Type: MEETING ABSTRACT

7/3,AB/132 (Item 13 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci
(c) 2002 Inst for Sci Info. All rts. reserv.

07296113 Genuine Article#: 141AW Number of References: 3 Title: Overexpression of the *hyaluronan* *receptor* RHAMM characterizes the malignant clone in multiple myeloma: Identification of three distinct RHAMM variants.
Author(s): Pilarski LM; Crainie M; Mant MJ; Belch AR
Corporate Source: UNIV ALBERTA,DEPT ONCOL & MED/EDMONTON/AB/CANADA/; CROSS CANC INST,/EDMONTON/AB T6G 1Z2/CANADA/
Journal: BLOOD, 1998, V92, N10,1,1 (NOV 15), P1055-1055
ISSN: 0006-4971 Publication date: 19981115
Publisher: W B SAUNDERS CO, INDEPENDENCE SQUARE WEST CURTIS CENTER, STE 300, PHILADELPHIA, PA 19106-3399
Language: English Document Type: MEETING ABSTRACT

7/3,AB/133 (Item 14 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci
(c) 2002 Inst for Sci Info. All rts. reserv.

07052466 Genuine Article#: 118GT Number of References: 0 Title: Molecular cloning of HAR, a novel human homolog of CD44 and putative *hyaluronic* *acid* *receptor*.
Author(s): Winkelmann JC; Basu S
Corporate Source: UNIV CINCINNATI,SCH MED/CINCINNATI//OH/
Journal: EXPERIMENTAL HEMATOLOGY, 1998, V26, N8 (AUG), P56-56 ISSN: 0301-472X Publication date:

19980800
Publisher: CARDEN JENNINGS PUBL CO LTD, BLAKE CTR, STE 200, 1224 W MAIN ST, CHARLOTTESVILLE, VA 22903
Language: English Document Type: MEETING ABSTRACT

7/3,AB/134 (Item 15 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci
(c) 2002 Inst for Sci Info. All rts. reserv.

06904443 Genuine Article#: 100XU Number of References: 0 Title: *Hyaluronan* *receptor* expression increases in fetal excisional skin wounds and correlates with fibroplasia - Discussion Author(s): Olutoye O; Lovvorn HN
Journal: JOURNAL OF PEDIATRIC SURGERY, 1998, V33, N7 (JUL), P1069-1070 ISSN: 0022-3468 Publication date: 19980700
Publisher: W B SAUNDERS CO, INDEPENDENCE SQUARE WEST CURTIS CENTER, STE 300, PHILADELPHIA, PA 19106-3399
Language: English Document Type: EDITORIAL MATERIAL

7/3,AB/135 (Item 16 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci
(c) 2002 Inst for Sci Info. All rts. reserv.

06750393 Genuine Article#: ZK302 Number of References: 0 Title: Expression of *hyaluronan* *receptor* CD44 and RHAMM in human gastric cancers
Author(s): Li H; Li JW; Gang Y; Guo L; Wu YH; Liu J; Martin H Corporate Source: SHENYANG MED COLL,DIV MOL BIOL/SHENYANG 110031//PEOPLES R CHINA/; IGEN,INST GENET/D-76021 KARLSRUHE//GERMANY/
Journal: FASEB JOURNAL, 1997, V11, N9,S (JUL 31), P3356-3356 ISSN: 0892-6638 Publication date: 19970731
Publisher: FEDERATION AMER SOC EXP BIOL, 9650 ROCKVILLE PIKE, BETHESDA, MD 20814-3998
Language: English Document Type: MEETING ABSTRACT

7/3,AB/136 (Item 17 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci
(c) 2002 Inst for Sci Info. All rts. reserv.

06484450 Genuine Article#: YU124 Number of References: 0 Title: PDGF-BB-stimulated smooth muscle cell (SMC) migration and chemotaxis is dependent on *hyaluronan* (*HA*) and the *HA* *receptor* RHAMM.
Author(s): Savani RC; Wentz E; Cui Z
Corporate Source: UNIV PENN,SCH MED, DIV NEONATOL/PHILADELPHIA//PA/19104 Journal: JOURNAL OF INVESTIGATIVE MEDICINE, 1998, V46, N1 (JAN), PA176-A176 ISSN: 1081-5589 Publication date: 19980100
Publisher: SLACK INC, 6900 GROVE RD, THOROFARE, NJ 08086
Language: English Document Type: MEETING ABSTRACT

7/3,AB/137 (Item 18 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci
(c) 2002 Inst for Sci Info. All rts. reserv.

06482951 Genuine Article#: YV140 Number of References: 0 Title: Expression of the *hyaluronic* *acid* *receptor*, CD44S, in ovarian epithelial cancer.
Author(s): Kayastha S; Werness BA
Corporate Source: ROSWELL PK CANC INST,DEPT PATHOL/BUFFALO//NY/ Journal: MODERN PATHOLOGY, 1998, V11, N1 (JAN), PA106-A106 ISSN: 0893-3952 Publication date: 19980100
Publisher: WILLIAMS & WILKINS, 351 WEST CAMDEN ST, BALTIMORE, MD 21201-2436 Language: English Document Type: MEETING ABSTRACT

7/3,AB/138 (Item 19 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci
(c) 2002 Inst for Sci Info. All rts. reserv.

05977695 Genuine Article#: XL493 Number of References: 45 Title: Unregulated renal tubular CD44, *hyaluronan*, and osteopontin in kdkd mice with interstitial nephritis (ABSTRACT AVAILABLE)
Author(s): Sibalic V; Fan X; Loffing J; Wuthrich RP (REPRINT) Corporate Source: UNIV ZURICH HOSP,DIV NEPHROL, RAMISTR 100/CH-8091 ZURICH//SWITZERLAND/ (REPRINT); UNIV ZURICH HOSP,DIV NEPHROL/CH-8091 ZURICH//SWITZERLAND/; UNIV ZURICH IRCHEL,INST PHYSIOL/CH-8057 ZURICH//SWITZERLAND/; UNIV ZURICH IRCHEL,INST ANAT/CH-8057 ZURICH//SWITZERLAND/
Journal: NEPHROLOGY DIALYSIS TRANSPLANTATION, 1997, V12, N7 (JUL), P 1344-1353
ISSN: 0931-0509 Publication date: 19970700
Publisher: OXFORD UNIV PRESS, GREAT CLARENDON ST, OXFORD, ENGLAND OX2 6DP Language: English Document Type: ARTICLE
Abstract: Background. The hyaluronan (*HA*) *receptor* CD44 is upregulated on parenchymal cells in various

inflammatory lesions and could play a role in immune injury. The purpose of the present study was to examine CD44 and its ligands HA and osteopontin (Opn) in a murine model of tubulointerstitial nephritis (TIN).

Methods. The expression of CD44 was investigated by immunofluorescence staining and RNA analysis in kidneys of kdkd mice with autoimmune TIN. The CD44 expression was then correlated with the location of its ligands HA and Opn.

Results. CD44 is expressed de novo by tubular epithelial cells (TEC) in areas of tubular injury in kdkd kidneys, but not in normal control kidneys. CD44 positive lymphocytes and macrophages also infiltrate the kidney in kdkd mice. RT-PCR and Southern blot analysis demonstrate that transcripts encoding standard and variant forms of CD44 are increased in kdkd mice with TIN. In parallel the CD44 ligand HA also accumulates in kdkd kidneys in the interstitial space, particularly in cortical areas of tubular injury. Furthermore, the expression of the chemotactic protein Opn is enhanced in kdkd kidney, predominantly in areas of tubular injury. Opn mRNA expression also increases markedly in kdkd kidneys compared with normal kidneys, and correlates with disease severity.

Conclusions. Prominent CD44 expression by TEC in areas of tubulointerstitial lesions is a characteristic feature of kdkd mice. The de novo appearance of CD44 on injured TEC might allow interaction with the ligands HA and Opn in vivo. Interaction of CD44 with these ligands could participate in the tubulointerstitial inflammatory response in kdkd mice.

7/3,AB/139 (Item 20 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci

05375623 Genuine Article#: VV145 Number of References: 87 Title: PP60(C-SRC) IS REQUIRED FOR CELL LOCOMOTION REGULATED BY THE *HYALURONAN* *RECEPTOR* RHAMM (Abstract Available) Author(s): HALL CL; LANGE LA; PROBER DA; ZHANG S; TURLEY EA Corporate Source: HOSP SICK CHILDREN,555 UNIV AVE/TORONTO/ON M5G 1X8/CANADA/; HOSP SICK CHILDREN/TORONTO/ON M5G 1X8/CANADA/; UNIV MANITOBA,MANITOBA INST CELL BIOL/WINNIPEG/MB R3E 0V9/CANADA/; UNIV MANITOBA,DEPT PEDIAT/WINNIPEG/MB R3E 0V9/CANADA/; UNIV MANITOBA,DEPT PHYSIOL/WINNIPEG/MB R3E 0V9/CANADA/ Journal: ONCOGENE, 1996, V13, N10 (NOV 21), P2213-2224
ISSN: 0950-9232

Language: ENGLISH Document Type: ARTICLE
Abstract: The tyrosine kinase pp60(c-src) has been implicated as a regulator of focal adhesion formation and cell spreading. Here we show that c-src also regulates cell motility and is a key component in the signaling pathway triggered by the motogenic *hyaluronan* *receptor* RHAMM, which has been shown to regulate focal adhesion turnover and to regulate ras. Fibroblasts derived from mice lacking src, (src (-/-), have a random locomotion rate that is significantly slower than the corresponding wild-type fibroblasts. Cell locomotion in these mutant cells is restored by the expression of c-src containing a functional kinase domain, but not by the expression of a kinase-deficient src or by a truncated src containing only functional SH2 and SH3 domains. RHAMM is also required for the restoration of src (-/-) cell locomotion. Thus, the motility of cells expressing c-src is reduced to src (-/-) levels by anti-RHAMM blocking antibodies while the cell locomotion of src (-/-) fibroblasts remains unaffected by anti-RHAMM antibodies. We predict that src acts downstream of RHAMM in the regulation of motility, since the expression of a dominant negative src significantly inhibits RHAMM-dependent ras and serum regulated cell locomotion, the expression of v-src enhances cell motility in a RHAMM independent fashion, and there is a physical and functional association between src and RHAMM in ras-transformed cells. However, we suggest that RHAMM regulates focal adhesion turnover via additional src-independent mechanisms. Thus, v-src is unable to turnover focal adhesions in the absence of RHAMM. These results directly demonstrate for the first time a role for src in the regulation of cell locomotion and confirm a key and complex role for src in the regulation of the actin cycle.

7/3,AB/140 (Item 21 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci

05285915 Genuine Article#: VM929 Number of References: 15 Title: THE CHARACTERIZATION OF A HUMAN RHAMM CDNA - CONSERVATION OF THE *HYALURONAN*-BINDING DOMAINS (Abstract Available) Author(s): WANG C; ENTWISTLE J; HOU GP; LI QA; TURLEY EA
Corporate Source: UNIV MANITOBA,MANITOBA INST CELL BIOL,DEPT PEDIAT & PHYSIOL,100 OLIVIA ST/WINNIPEG/MB R3E 0V9/CANADA/; UNIV MANITOBA,MANITOBA INST CELL BIOL,DEPT PEDIAT & PHYSIOL/WINNIPEG/MB R3E 0V9/CANADA/
Journal: GENE, 1996, V174, N2 (OCT 3), P299-306
ISSN: 0378-1119

Language: ENGLISH Document Type: ARTICLE
Abstract: A full-length human RHAMM cDNA clone was isolated by a combination of screening a human breast cDNA expression library with the murine RHAMM 2 cDNA as well as 5' RACE and RT-PCR using messenger RNA from human breast cell line (MCF-10A). The full-length cDNA contained 725 aa that encoded an 84 kDa protein. Although the coding region of the human RHAMM cDNA resembles the murine RHAMM v4, it has additional unique N-terminal (489 bp) and C-terminal (33 bp) regions. Also, only 1 of 5 repeat sequences encoded in the murine cDNA are present in human cDNA. The overall homology between the overlapping region of human and mouse RHAMM v4 cDNA clone is 85%, but the HA binding motif (B[X(7)]B), shown to be critical for the signaling capability of this receptor, is 100% conserved.

7/3,AB/141 (Item 22 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci
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05278575 Genuine Article#: VL285 Number of References: 0 Title: CD44 (*HYALURONAN* *RECEPTOR*) IN THE HEPATIC SINUSOIDAL ENDOTHELIAL-CELL DECREASES IN LIVER-CIRRHOSIS
Author(s): UENO T; TAMAKI S; TORIMURA T; SAKAMOTO M; SAKATA R; INUZUKA S; SATA M; TANIKAWA K
Corporate Source: KURUME UNIV,SCH MED,DEPT MED 2/KURUME/FUKUOKA 830/JAPAN/ Journal: HEPATOLOGY, 1996, V24, N4 (OCT), P1861
ISSN: 0270-9139
Language: ENGLISH Document Type: MEETING ABSTRACT

7/3,AB/142 (Item 23 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci
(c) 2002 Inst for Sci Info. All rts. reserv.

05276757 Genuine Article#: VL285 Number of References: 0 Title: TARGETED GENE DELIVERY TO LIVER ENDOTHELIAL-CELLS BY *HYALURONAN* *RECEPTOR*-MEDIATED ENDOCYTOSIS
Author(s): TAKEI Y; KAWANO S; OKUMURA S; NAGAI H; OMAE A; OSHITA M; ENOMOTO N; HASHIMOTO M; MAKINO Y; KINOSHITA M; YAMANAKA H; ASAYAMA S; NOGAWA M; MARUYAMA A; AKAIKE T
Corporate Source: OSAKA UNIV,SCH MED,DEPT MED 1/SUITA/OSAKA 565/JAPAN/; TOKYO INST TECHNOL,FAC BIOSCI & BIOTECHNOL,DEPTBIOMOL ENGN/YOKOHAMA/KANAGAWA 227/JAPAN/
Journal: HEPATOLOGY, 1996, V24, N4 (OCT), P39
ISSN: 0270-9139
Language: ENGLISH Document Type: MEETING ABSTRACT

7/3,AB/143 (Item 24 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci
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04890098 Genuine Article#: UQ220 Number of References: 45 Title: OVEREXPRESSION OF CD44 IN P185(NEU)-TRANSFECTED NIH3T3 CELLS PROMOTES AN UP-REGULATION OF *HYALURONIC* ACID-MEDIATED MEMBRANE-CYTOSKELETON INTERACTION AND CELL-ADHESION (Abstract Available)
Author(s): ZHU D; BOURGUIGNON L
Corporate Source: UNIV MIAMI,SCH MED,DEPT CELL BIOL & ANAT/MIAMI//FL/33101; UNIV MIAMI,SCH MED,DEPT CELL BIOL & ANAT/MIAMI//FL/33101
Journal: ONCOGENE, 1996, V12, N11 (JUN 6), P2309-2314
ISSN: 0950-9232
Language: ENGLISH Document Type: ARTICLE
Abstract: CD44 is a transmembrane glycoprotein known to bind hyaluronic acid (HA) in its extracellular domain and to contain at least one ankyrin-binding site in its cytoplasmic domain. In this study we have examined CD44 expression in a mouse fibroblast cell line transfected with the p185(neu) oncogene cDNA. The results of RT-PCR and Southern blot analyses reveal that CD44s (CD44 standard form) transcript is expressed in both p185(neu)-transfected cells and untransfected cells. Using surface iodination, anti-CD44 immunoprecipitation and immune-binding assays, we have found that the number of CD44s molecules expressed on the surface of p185(neu)-transfected cells are at least 4.5-fold higher than those detected on untransfected cells. Overexpression of surface CD44s in p185(neu)-transfected cells results in a dramatic enhancement of HA-mediated cell adhesion. Scatchard plot analysis indicates that CD44s in p185(neu)-transfected cells binds directly and specifically to ankyrin. The binding affinity between CD44s and ankyrin in p185(neu)-transfected cells (K-d approximate to 0.19 nM) appears to be somewhat higher than that found in the untransfected cells (K-d approximate to 0.30 nM). Double immunofluorescence staining and confocal microscopic analyses indicate that HA induces the *HA* *receptor* (i.e. CD44s) to form adhesion plaque-like structures, and causes an accumulation of intracellular ankyrin directly underneath *HA* *receptor* (CD44s)-adhesion plaque-like structures in p185(neu)-transfected cells (but not in untransfected cells). These findings suggest

that overexpression of CD44s and up-regulation of CD44s-ankyrin interaction by p185(neu) oncogene may be one of the pre-requisite steps in regulating tumor cell behavior.

7/3,AB/144 (Item 25 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci
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04841651 Genuine Article#: UK861 Number of References: 0 Title: PURIFICATION OF THE RAT-LIVER SINUSOIDAL ENDOTHELIAL-CELL (LEC) *HYALURONAN* *RECEPTOR*
Author(s): ZHOU B; WEIGEL P
Corporate Source: UNIV OKLAHOMA,HLTH SCI CTR,DEPT BIOCHEM & MOLECBIOL/OKLAHOMA CITY//OK/73190
Journal: FASEB JOURNAL, 1996, V10, N6 (APR 30), P566
ISSN: 0892-6638
Language: ENGLISH Document Type: MEETING ABSTRACT

7/3,AB/145 (Item 26 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci
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04744623 Genuine Article#: UD238 Number of References: 0 Title: NITRIC OXIDE-MEDIATED MACROPHAGE CHEMOTAXIS IS DEPENDENT ON *HYALURONAN* (*HA*) AND THE *HA* *RECEPTOR* RHAMM Author(s): HANLONDEARMAN A; SAVANI RC
Corporate Source: UNIV MANITOBA,DEPT PEDIAT/WINNIPEG/MB R3T 2N2/CANADA/; UNIV MANITOBA,MANITOBA INST CELL BIOL/WINNIPEG/MB R3T 2N2/CANADA/ Journal: PEDIATRIC RESEARCH, 1996, V39, N4 (APR), P1989
ISSN: 0031-3998
Language: ENGLISH Document Type: MEETING ABSTRACT

7/3,AB/146 (Item 27 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci
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04744609 Genuine Article#: UD238 Number of References: 0 Title: SYSTEMIC AND INTRATRACHEAL STEROIDS DECREASE THE PRODUCTION OF *HYALURONAN* (*HA*) AND REDUCE THE EXPRESSION OF THE *HA* *RECEPTOR* RHAMM DURING BLEOMYCIN-INDUCED PULMONARY INFLAMMATION Author(s): FAJARDO C; HUSSAIN A; WANG P; SAVANI RC
Corporate Source: UNIV MANITOBA,DEPT PEDIAT/WINNIPEG/MB R3T 2N2/CANADA/; UNIV MANITOBA,MANITOBA INST CELL BIOL/WINNIPEG/MB R3T 2N2/CANADA/ Journal: PEDIATRIC RESEARCH, 1996, V39, N4 (APR), P1975
ISSN: 0031-3998
Language: ENGLISH Document Type: MEETING ABSTRACT

7/3,AB/147 (Item 28 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci
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04612805 Genuine Article#: TT801 Number of References: 0 Title: POLYMER-BASED AFFINITY PRECIPITATION SEPARATION OF THE PRESUMPTION *HYALURONAN* *RECEPTOR* - CD44
Author(s): SHETTY V; BERG S; LE A; BERTOLAMI CN; DING Z; HOFFMAN A Corporate Source: UNIV CALIF LOS ANGELES/LOS ANGELES//CA/00000; UNIV WASHINGTON/SEATTLE//WA/98195
Journal: JOURNAL OF DENTAL RESEARCH, 1996, V75, NSI, P89
ISSN: 0022-0345
Language: ENGLISH Document Type: MEETING ABSTRACT

7/3,AB/148 (Item 29 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci
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04534281 Genuine Article#: TQ513 Number of References: 16 Title: LOCALIZATION OF *HYALURONAN* AND THE *HYALURONAN* *RECEPTOR* ICAM-1 IN RHEUMATOID SYNOVIA - A HISTOCHEMICAL-STUDY Author(s): GUSTAFSON S; ENGSTROMLAURENT A; WIKSTROM T; GUSTAFSON AM Corporate Source: UNIV UPPSALA,DEPT MED & PHYSIOL CHEM,POB 575/S-75123 UPPSALA//SWEDEN/; CTR HOSP FALUN,DEPT RHEUMATOL/S-79182 FALUN//SWEDEN/ Journal: ACTA ORTHOPAEDICA SCANDINAVICA, 1995, V66, S266 (OCT), P162-164 ISSN: 0001-6470
Language: ENGLISH Document Type: ARTICLE

7/3,AB/149 (Item 30 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci
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04524007 Genuine Article#: TK885 Number of References: 55 Title: REGULATION OF CD44 BINDING TO *HYALURONAN* BY GLYCOSYLATION OF VARIABLY SPLICED EXONS (Abstract Available)
Author(s): BENNETT KL; MODRELL B; GREENFIELD B;

BARTOLAZZI A; STAMENKOVIC I ; PEACH R; JACKSON DG; SPRING F; ARUFFO A
Corporate Source: BRISTOL MYERS SQUIBB PHARMACEUT RES INST,3005 1ST AVE/SEATTLE//WA/98121; MASSACHUSETTS GEN HOSP,DEPT PATHOL/BOSTON//MA/02114; JOHN RADCLIFFE HOSP,INST MOLEC MED,MOLEC IMMUNOL GRP/OXFORD OX3 9DU//ENGLAND/; REFERENCE LAB,INT BLOOD GRP/BRISTOL BS10 5ND/AVON/ENGLAND/
Journal: JOURNAL OF CELL BIOLOGY, 1995, V131, N6 (DEC), P1623-1633 ISSN: 0021-9525
Language: ENGLISH Document Type: ARTICLE
Abstract: The hyaluronan (HA)-binding function (lectin function) of the leukocyte homing receptor, CD44, is tightly regulated. Herein we address possible mechanisms that regulate CD44 isoform-specific Hii binding. Binding studies with melanoma transfectants expressing CD44H, CD44E, or with soluble immunoglobulin fusions of CD44H and CD44E (CD44H-Rg, CD44E-Rg) showed that although both CD44 isoforms can bind HA, CD44H binds HA more efficiently than CD44E. Using CD44-Rg fusion proteins we show that the variably spliced exons in CD44E, V8-V10, specifically reduce the lectin function of CD44, while replacement of V8-V10 by an ICAM-1 immunoglobulin domain restores binding to a level comparable to that of CD44H. Conversely, CD44 bound HA very weakly when exons V8-V10 were replaced with a CD34 mucin domain, which is heavily modified by O-linked glycans. Production of CD44E-Rg or incubation of CD44E-expressing transfectants in the presence of an O-linked glycosylation inhibitor restored HA binding to CD44H-Rg and to cell surface CD44H levels, respectively. We conclude that differential splicing provides a regulatory mechanism for CD44 lectin function and that this effect is due in part to O-linked carbohydrate moieties which are added to the Ser/Thr rich regions encoded by the variably spliced CD44 exons. Alternative splicing resulting in changes in protein glycosylation provide a novel mechanism for the regulation of lectin activity.

7/3,AB/150 (Item 31 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci
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04353590 Genuine Article#: RY581 Number of References: 44 Title: N-TERMINAL AND CENTRAL REGIONS OF THE HUMAN CD44 EXTRACELLULAR DOMAIN PARTICIPATE IN CELL-SURFACE *HYALURONAN*-BINDING (Abstract Available)
Author(s): LIAO HX; LEE DM; LEVESQUE MC; HAYNES BF
Corporate Source: DUKE UNIV,MED CTR,DUKE ARTHRITIS CTR,DEPT MED,BOX 3258/DURHAM//NC/27710
Journal: JOURNAL OF IMMUNOLOGY, 1995, V155, N8 (OCT 15), P3938-3945 ISSN: 0022-1767
Language: ENGLISH Document Type: ARTICLE
Abstract: CD44 molecules are cell surface receptors for hyaluronan (HA). To define regions of the extracellular domain of CD44 that are important for HA binding, we have studied the ability of HA-blocking CD44 mAbs to bind to CD44 from a variety of sources. Five CD44 mAbs (5F12, BRIC235, 3F12, BU-75, and HP2/9) of 21 studied were identified that at least partially blocked FITC-labeled HA (HA-FITC) binding to the standard form of CD44 (CD44S) in CD44-transfected jurkat cells. Analysis of reactivity of HA-blocking CD44 mAbs defined three distinct epitopes. Lack of reactivity of mAb 5F12 with a CD44 fusion protein (CD44-Rg) containing an N-terminal truncation of 20 amino acids (aa), as well as reactivity of mAb 5F12 with an N-terminal CD44 synthetic peptide (CD44-9A), demonstrated that the N-terminal proximal region of CD44 (aa 1 to 20) was involved in mAb 5F12 binding. A mutant cell line, CEM-NKR, derived from the T-ALL cell line, GEM, did not bind mAb 5F12 nor bind HA, whereas wild-type CEM did bind mAb 5F12 and HA. Sequence analysis of wild-type CEM and CEM-NKR CD44 cDNA demonstrated a G to A point mutation at position 575 in the CD44 cDNA of CEM-NKR, resulting in an arginine to histidine mutation at aa position 154. Taken together, our studies demonstrated that there are three epitopes to which HA-blocking mAbs bind in the extracellular domain of CD44, and that the CD44 N-terminal proximal and central regions are two regions in the extracellular domain of CD44 that may interact and either mediate or regulate HA binding to cell surface CD44.

7/3,AB/151 (Item 32 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci
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04267203 Genuine Article#: QP082 Number of References: 0 Title: PEPTIDES DERIVED FROM THE *HYALURONAN* *RECEPTOR* RHAMM PREVENT INFLAMMATION AND FIBROSIS IN-VIVO - POTENTIAL THERAPY FOR PULMONARY FIBROSIS
Author(s): SAVANI RC; SIMONS FE; LIU P; SANGSTER K; KHALIL N; TURLEY EA Corporate Source: UNIV MANITOBA,DEPT PEDIAT/WINNIPEG/MB R3T 2N2/CANADA/; UNIV MANITOBA,MANITOBA INST CELL BIOL/WINNIPEG/MB R3T 2N2/CANADA/
Journal: PEDIATRIC RESEARCH, 1995, V37, N4 (APR), PA348
ISSN: 0031-3998

Language: ENGLISH Document Type: MEETING ABSTRACT

7/3,AB/152 (Item 33 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci
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04158605 Genuine Article#: RL098 Number of References: 66 Title: GLYCOSYLATION OF CD44 NEGATIVELY REGULATES ITS RECOGNITION OF *HYALURONAN* (Abstract Available)
Author(s): KATOH S; ZHENG Z; ORITANI K; SHIMOZATO T; KINCADE PW Corporate Source: OKLAHOMA MED RES FDN,825 NE 13TH ST/OKLAHOMA CITY//OK/73104; OKLAHOMA MED RES FDN/OKLAHOMA CITY//OK/73104 Journal: JOURNAL OF EXPERIMENTAL MEDICINE, 1995, V182, N2 (AUG 1), P419-429 ISSN: 0022-1007
Language: ENGLISH Document Type: ARTICLE
Abstract: Although CD44 is expressed on a wide variety of cell types, few of them use it to recognize the ligand hyaluronan (HA). A glycosylation-defective clone of Chinese hamster ovary cells (Lee and) bound HA, demonstrating that complete processing of glycoproteins with addition of a full complement of sialic acid is not required. On the contrary, subsequent findings revealed that complex sugars on CD44 can actually inhibit ligand recognition. Two subclones of wild-type Chinese hamster ovary cells with similar amounts of surface CD44 were isolated on the basis of HA binding and found to differ with respect to CD44 size as well as staining with fluorescent lectins. Treatment of the nonbinding clone with tunicamycin reduced the size of the protein and allowed the cells to recognize HA via CD44. This function was also induced by treatment with deglycosylating enzymes (either a mixture of endoglycosidase F and N-glycosidase F or neuraminidase alone). A possible role for glycosylation in regulation of adhesion was then sought with a series of normal and transformed murine cells. Disruption of glycosylation or treatment with deglycosylating enzymes did not induce ligand binding in an interleukin 7-dependent pre-B cell line, and splenic B cells also appeared to be in an inactive state. Some normal B cells acquired the ability to recognize HA after stimulation with lipopolysaccharide or interleukin 5 and had distinctive surface characteristics (loss of immunoglobulin D and acquisition of CD43). An additional subset of activated cells might have been in a transitional state, because the cells bound ligand after neuraminidase treatment. The ligand-binding ability of a purified CD44-immunoglobulin fusion protein dramatically increased after neuraminidase treatment. Thus, differential glycosylation of this molecule is sufficient to influence its recognition function. Cell adhesion involving HA can be regulated by multiple mechanisms, one of which involves variable glycosylation of CD44.

7/3,AB/153 (Item 34 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci
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04152853 Genuine Article#: RK161 Number of References: 59 Title: MONOCLONAL-ANTIBODIES TO CD44 AND THEIR INFLUENCE ON *HYALURONAN* RECOGNITION (Abstract Available)
Author(s): ZHENG Z; KATOH S; HE Q; ORITANI K; MIYAKE K; LESLEY J; HYMAN R; HAMIK A; PARKHOUSE RME; FARR AG; KINCADE PW Corporate Source: OKLAHOMA MED RES FDN,IMMUNOBIOL & CANC PROGRAM,825 NE 13TH ST/OKLAHOMA CITY//OK/73104; OKLAHOMA MED RES FDN,IMMUNOBIOL & CANC PROGRAM/OKLAHOMA CITY//OK/73104; SALK INST/SAN DIEGO//CA/92186; INST ANIM HLTH/WOKING/SURREY/ENGLAND/; UNIV WASHINGTON,DEPT BIOL STRUCT/SEATTLE//WA/98195
Journal: JOURNAL OF CELL BIOLOGY, 1995, V130, N2 (JUL), P485-495 ISSN: 0021-9525
Language: ENGLISH Document Type: ARTICLE
Abstract: Antibodies to CD44 have been used to inhibit a variety of processes which include lymphohemopoiesis, lymphocyte migration, and tumor metastasis. Some, but not all, CD44-mediated functions derive from its ability to serve as a receptor for hyaluronan (HA). However, sites on CD44 that interact with either ligands or antibodies are poorly understood. Interspecies rat/mouse CD44 chimeras were used to analyze the specificity of 25 mAbs and to determine that they recognize at least seven epitopes. Amino acid substitutions that resulted in loss of antibody recognition were all located in the region of homology to other cartilage link family proteins. While at least five epitopes were eliminated by single amino acid replacements, multiple residues had to be changed to destroy binding by other antibodies. One antibody was sensitive to changes in any of three separate parts of the molecule and some antibodies to distinct epitopes cross-blocked each other. Certain antibodies had the ability to increase HA binding by lymphocytes but this did not correlate absolutely with antibody specificity and was only partially attributable to CD44 cross-linking. Antibodies that consistently blocked HA recognition were all sensitive to amino acid changes within a short stretch of CD44. Such blocking antibodies interacted with CD44 more strongly than ligand in competition experiments. One large group of antibodies blocked ligand binding, but only with a particular cell, line. This detailed analysis adds to our understanding of

functional domains within CD44 and requirements for antibodies to influence recognition of one ligand.

7/3,AB/154 (Item 35 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci
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04138744 Genuine Article#: RH245 Number of References: 46 Title: BIOTINYLATED *HYALURONIC*-ACID AS A PROBE FOR IDENTIFYING *HYALURONIC* ACID-BINDING PROTEINS (Abstract Available) Author(s): YANG BH; YANG BL; GOETINCK PF
Corporate Source: HARVARD UNIV,MASSACHUSETTS GEN HOSP,SCH MED,CUTANEOUS BIOL RES CTR/BOSTON//MA/02129; HARVARD UNIV,MASSACHUSETTS GEN HOSP,SCH MED,CUTANEOUS BIOL RES CTR/BOSTON//MA/02129
Journal: ANALYTICAL BIOCHEMISTRY, 1995, V228, N2 (JUL 1), P299-306 ISSN: 0003-2697
Language: ENGLISH Document Type: ARTICLE
Abstract: The glycosaminoglycans hyaluronan (HA), heparin, and chondroitin sulfate were biotinylated using biotin-x-hhydrazide
(biotin-epsilon-aminocaproyl hydrozyde) in conjunction with N-ethyl-N'-(3-dimethylaminopropyl)carbodiimide hydrochloride, an activating agent for carboxyl groups. The biotin-x-hydrazide was shown to be coupled directly to the glycosaminoglycans in enzymatic digestions and competition experiments. The biotinylated HA was shown to bind to link protein and receptor for hyaluronic acid-mediated motility, two proteins known to bind HA. The labeled HA was used as a probe to detect known HA-binding proteins in chicken cartilage extract and to identify new HA-binding motifs in the G3 domain of the proteoglycan aggrecan. The significance of the biotinylation of HA, heparin, and chondroitin sulfate A are discussed. (C) 1995 Academic Press, Inc.

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04129590 Genuine Article#: RG362 Number of References: 25 Title: BIOTINYLATED *HYALURONAN* AS A PROBE FOR DETECTION OF BINDING-PROTEINS IN CELLS AND TISSUES (Abstract Available) Author(s): YU Q; TOOLE BP
Corporate Source: TUFTS UNIV,SCH MED,DEPT ANAT & CELLULAR BIOL,136 HARRISON AVE/BOSTON//MA/02111; TUFTS UNIV,SCH MED,DEPT ANAT & CELLULAR BIOL/BOSTON//MA/02111
Journal: BIOTECHNIQUES, 1995, V19, N1 (JUL), P122&
ISSN: 0736-6205
Language: ENGLISH Document Type: ARTICLE
Abstract: A convenient and reliable method for preparing and using biotinylated hyaluronan for detection of hyaluronan-binding proteins is described. The biotinylated hyaluronan can be used to detect binding proteins in transblots after electrophoresis or as a histological probe for localization of binding proteins in cultured cells and tissue sections.

7/3,AB/156 (Item 37 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci
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04024775 Genuine Article#: QZ754 Number of References: 100 Title: *CHONDROITIN* SULFATE PROTEOGLYCANS IN THE DEVELOPING CEREBRAL-CORTEX - THE DISTRIBUTION OF NEUROCAN DISTINGUISHES FORMING AFFERENT AND EFFERENT AXONAL PATHWAYS (Abstract Available) Author(s): MILLER B; SHEPPARD AM; BICKNESE AR; PEARLMAN AL Corporate Source: WASHINGTON UNIV,SCH MED,DEPT CELL BIOL,BOX 8228,660 S EUCLID AVE/ST LOUIS//MO/63110; WASHINGTON UNIV,SCH MED,DEPT CELL BIOL/ST LOUIS//MO/63110; WASHINGTON UNIV,SCH MED,DEPT NEUROL/ST LOUIS//MO/63110; WASHINGTON UNIV,SCH MED,DEPT PEDIAT/ST LOUIS//MO/63110 Journal: JOURNAL OF COMPARATIVE NEUROLOGY, 1995, V355, N4 (MAY 15), P 615-628
ISSN: 0021-9967
Language: ENGLISH Document Type: REVIEW
Abstract: The first thalamocortical axons to arrive in the developing cerebral cortex traverse a pathway that is separate from the adjacent intracortical pathway for early efferents, suggesting that different molecular signals guide their growth. We previously demonstrated that the intracortical pathway for thalamic axons is centered on the subplate (Bicknese et al. [1994] J. Neurosci. 14:3500-3510), which is rich in chondroitin sulfate proteoglycans (CSPGs; Sheppard et al. [1991] J. Neurosci. 11:3928-3942), whereas efferent axons cross the subplate to exit in a zone containing much less CSPG. To define the molecular composition of the subplate further, we used antibodies against CSPG core proteins and chondroitin sulfate disaccharides in an immunohistochemical analysis of their distribution in the developing neocortex of the rat. Immunolabeling for neurocan, a central nervous system-specific CSPG (Rauch et al. [1992] J. Biol. Chem. 267:19537-19547), and for chondroitin 6-sulfate and unsulfated chondroitin becomes prominent in the subplate before the arrival of thalamic afferents. Immunolabeling is initially

sparse in the cortical plate but appears later in maturing cortical layers. A postnatal decline in immunolabeling occurs uniformly for most proteoglycans, but, in the somatosensory cortex, labeling for neurocan, phosphacan, and chondroitin 4- and B-sulfate declines in the centers of the whisker barrels before the walls. In contrast to neurocan, immunolabeling for other proteoglycans is either uniformly distributed (syndecan-1, N-syndecan, 5F3, phosphacan, chondroitin 4-sulfate), restricted to axons (PGM1), distributed exclusively on nonneuronal elements (2D6, NG2, and CD44), or undetectable (9.2.27, aggrecan, decorin). Thus, neurocan is a candidate molecule for delineating the intracortical pathway of thalamocortical axons and distinguishing it from that of cortical efferents. (C) 1995 Wiley-Liss, Inc.

7/3,AB/157 (Item 38 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci
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04007648 Genuine Article#: QY506 Number of References: 27 Title: ROLE OF CD44 CYTOPLASMIC DOMAIN IN *HYALURONAN*-BINDING (Abstract Available)
Author(s): PERSCHL A; LESLEY J; ENGLISH N; TROWBRIDGE I; HYMAN R Corporate Source: SALK INST,DEPT CANC BIOL,POB 85800/SAN DIEGO//CA/92186; SALK INST,DEPT CANC BIOL/SAN DIEGO//CA/92186
Journal: EUROPEAN JOURNAL OF IMMUNOLOGY, 1995, V25, N2 (FEB), P495-501 ISSN: 0014-2980
Language: ENGLISH Document Type: ARTICLE
Abstract: The hyaluronan (HA) binding activity of mutant CD44 constructs expressed in AKR1 T-lymphoma cells was evaluated by flow cytometry using fluorescein-conjugated HA (Fl-HA). Previous studies showed that wild-type hematopoietic CD44 bound Fl-HA when expressed in AKR1, but that truncated ''tailless'' CD44, lacking all but six amino acids of the cytoplasmic domain, did not bind. Here,we show that a disulfide-bonded dimer of CD44, formed by substituting the transmembrane region of CD3 xi chain for that of CD44, binds Fl-HA, even when the cytoplasmic domain of the CD44 dimer is absent. We conclude that dimerization of CD44 abrogates the requirement for the cytoplasmic domain, suggesting that the cytoplasmic domain of CD44 may contribute to HA binding by promoting CD44 clustering. These results suggest that changes in the distribution of CD44 on the cell surface, induced by molecular interactions either from within the cell or from outside, may regulate its role as a receptor.

Further studies sought to localize the region of the CD44 cytoplasmic domain contributing to HA binding by the construction of a series of cytoplasmic domain truncation mutants and internal deletion mutants. All of the mutant CD44 molecules bound Fl-HA similarly to wild-type CD44. Thus, it was not possible to assign the function mediating HA binding to a specific region of the cytoplasmic domain, suggesting either that multiple regions of the cytoplasmic domain can promote enhancement of HA binding, or that the role of the cytoplasmic domain in mediating this function does not require a specific amino acid sequence.

7/3,AB/158 (Item 39 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci
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03986311 Genuine Article#: QM915 Number of References: 0 Title: AGE-RELATED-CHANGES IN THE EXPRESSION OF *HYALURONAN* *RECEPTOR* - CD44 - AND HYALURONATE SYNTHASE IN HUMAN TRABECULAR MESHWORK
Author(s): MAYANIL CSK; GOOSSENS W; KNEPPER PA
Corporate Source: NORTHWESTERN UNIV,SCH MED,OCULOCEREBROSPINAL INVEST LAB/CHICAGO//IL/60611
Journal: INVESTIGATIVE OPHTHALMOLOGY & VISUAL SCIENCE, 1995, V36, N4 (MAR 15), PS129
ISSN: 0146-0404
Language: ENGLISH Document Type: MEETING ABSTRACT

7/3,AB/159 (Item 40 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci
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03979283 Genuine Article#: QW497 Number of References: 38 Title: CYTOCHEMICAL-LOCALIZATION OF *HYALURONIC*-ACID IN HUMAN SYNOVIUM WITH SPECIAL REFERENCE TO ITS POSSIBLE PROCESS OF DEGRADATION (Abstract Available)
Author(s): ASARI A; KURIYAMA S; KOMINAMI E; UCHIYAMA Y
Corporate Source: SEIKAGAKU CORP,TOKYO RES INST,1253 TATENO 3-CHOME/HIGASHIYAMATO/TOKYO 207/JAPAN/; NIHONKOHKAN HOSP,DEPT ORTHOPED SURG/KAWASAKI/KANAGAWA/JAPAN/; JUNTENDO UNIV,SCH MED,DEPT BIOCHEM/TOKYO 113//JAPAN/; IWATE MED UNIV,SCH MED,DEPT CELL BIOL & NEUROANAT/MORIOKA/IWATE/JAPAN/
Journal: ARCHIVES OF HISTOLOGY AND CYTOLOGY, 1995, V58, N1 (MAR), P65-76 ISSN: 0004-0681
Language: ENGLISH Document Type: ARTICLE

Abstract: Fibroblast-like type B cells are known to produce hyaluronic acid (HA), but the process of its degradation remains unknown, In order to examine the possible route for the degradation of HA in normal human synovium, histochemical and immunohistochemical techniques were applied to the synovial tissue, using biotinylated HA binding region (HABR) and antibodies against CD44 and cathepsin B, Reaction products for HA and CD44 were detected on the cell surface of all synovial lining cells, while half of these lining cells contained intracellular stainings of HA and CD44, Electron microscopically, the lining cells containing intracellularly stained HA and CD44 extended cytoplasmic processes (type A cells), while the other lining cells possessed a smooth cell surface (type B cells), By light microscopic double staining, the intracellular stainings of HA and CD44 appeared co-localized in the cells immunopositive for cystatin beta, an endogenous cysteine proteinase inhibitor which has been shown to be localized in alveolar macrophages and osteoclasts. Moreover, these intracellular stainings of HA and CD44 were co-localized with immunodeposits for cathepsin B, a representative cysteine proteinase in lysosomes, In the extracellular staining of HA, dot-like reaction products appeared on fibrous structures with a periodicity of 41.7 nm, These results suggest that Type A cells in the normal human synovium participate in the degradation of HA by its CD44 mediated intake, Furthermore, HA may be closely associated with fibrous structures, probably type III collagen molecules.

7/3,AB/160 (Item 41 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci
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03954341 Genuine Article#: BC87X Number of References: 55 Title: *HYALURONIC*-ACID RECEPTORS
Author(s): STAMENKOVIC I; ARUFFO A
Corporate Source: MASSACHUSETTS GEN HOSP,DEPT PATHOL/BOSTON//MA/02129; HARVARD UNIV,MASSACHUSETTS GEN HOSP,SCH MED/BOSTON//MA/02129; BRISTOL MYERS SQUIBB CO,PHARMACEUT RES INST/SEATTLE//WA/98121
Journal: METHODS IN ENZYMOLOGY, 1994, V245, P195-216
ISSN: 0076-6879
Language: ENGLISH Document Type: REVIEW

7/3,AB/161 (Item 42 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci
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03946764 Genuine Article#: QU418 Number of References: 30 Title: *HYALURONAN* (HYAL-BV-5200) INHIBITS NEOINTIMAL MACROPHAGE INFLUX AFTER BALLOON-CATHETER INDUCED INJURY IN THE CHOLESTEROL-FED RABBIT (Abstract Available)
Author(s): FERNS GAA; KONNEH M; RUTHERFORD C; WOOLAGHAN E; ANGGARD EE Corporate Source: UNIV LONDON ST BARTHOLOMEWS HOSP & MED COLL,WILLIAM HARVEY RES INST,CHARTERHOUSE SQ/LONDON EC1M6BQ//ENGLAND/; UNIV LEICESTER,GLENFIELD GEN HOSP,DEPT CHEM PATHOL/LEICESTER LE3 9QP/LEICS/ENGLAND/
Journal: ATHEROSCLEROSIS, 1995, V114, N2 (APR 24), P157-164 ISSN: 0021-9150
Language: ENGLISH Document Type: ARTICLE
Abstract: Hyaluronan is a glycosaminoglycan, elaborated by several cell types, and is a major constituent of the extracellular matrix. Recent studies suggest that hyaluronan influences cell migration and proliferation. At high concentrations, it has been shown to inhibit macrophage migration in vitro. We have investigated the effects of hyaluronan administration on neo-intimal lesion development following balloon catheter injury of the common carotid artery in the cholesterol-fed New Zealand White rabbit. Hyaluronan, administered as sodium hyaluronate at the time of surgery and daily until sacrifice, 2 weeks later, reduced the absolute neo-intimal response to injury by 42% (117 +/- 16 mu m to 68 +/- 11 mu m; P < 0.05), and the intima-media ratio by 35% (0.91 +/- 0.10 to 0.59 +/- 0.11; P < 0.05). This was associated with a 62% reduction in intimal macrophage content (8.63 +/- 1.85% to 3.25 +/- 1.05%; P < 0.02). At the time of killing, serum cholesterol levels and weight gain were comparable between the groups of animals receiving a cholesterol diet (P > 0.05). In both groups mean serum cholesterol levels at the time of the balloon injury and killing were significantly greater than at entry (P < 0.001), and significantly higher than in a group receiving control chow (P < 0.001). These data suggest that the effect of hyaluronic acid on neo-intimal size may be mediated, in part, by an inhibition of monocyte/macrophage influx, and support the view that hyaluronan impairs monocyte migration.

7/3,AB/162 (Item 43 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci
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03903936 Genuine Article#: QR070 Number of References: 31 Title: *HYALURONIC*-ACID ENHANCES CELL-PROLIFERATION DURING EOSINOPOIESIS THROUGH THE CD44 SURFACE-ANTIGEN (Abstract Available) Author(s): HAMANN KJ; DOWLING TL; NEELEY SP; GRANT JA; LEFF AR Corporate Source: UNIV CHICAGO,MED CTR,ASTHMA & ALLERG DIS RES

CTR,DEPT MED,PULM & CRIT CARE MED SECT/CHICAGO//IL/60637; UNIV CHICAGO,DEPT PHYSIOL & PHARMACOL SCI/CHICAGO//IL/60637; UNIV CHICAGO,COMM CELL PHYSIOL,DIV BIOL SCI/CHICAGO//IL/60637
Journal: JOURNAL OF IMMUNOLOGY, 1995, V154, N8 (APR 15), P4073-4080 ISSN: 0022-1767
Language: ENGLISH Document Type: ARTICLE
Abstract: We examined the effect oi hyaluronic acid in promoting proliferation of undifferentiated progenitor cells through the CD44 receptor during eosinopoiesis in vitro. Undifferentiated umbilical cord blood cells were purified on the first day to isolate primitive progenitor cells expressing the CD34 hemopoietic surface marker. Culture in wells coated with 100 mu g/ml hyaluronic acid caused a 198 +/- 28.7% augmentation of proliferation of CD34(+) progenitor. cells at 3 wk ($p < 0.01$). By contrast, concentrations of hyaluronic acid >10 mu g/ml inhibited proliferation of unfractionated cord blood mononuclear cells. The augmented proliferation of precursor cells caused by hyaluronic acid was associated with complete (93.0 +/- 5.12%) differentiation to eosinophil morphology. By contrast, concentrations of hyaluronic acid greater than or equal to 10 mu g/ml inhibited eosinophilic differentiation of unfractionated mononuclear cells. Wright-Giemsa staining demonstrated 95.4 +/- 2.92% eosinophils for CD34(+) cells cultured for 3 wk without hyaluronic acid (control) and 93.8 +/- 5.11% for CD34(+) cells cultured in hyaluronic acid-coated wells (100 mu g/ml); for unfractionated cells, 94.0 +/- 3.02% demonstrated eosinophilic morphology in control wells at 3 wk vs 55.4 +/- 8.34% in hyaluronic acid-coated (100 mu g/ml) wells ($p < 0.05$). Augmented proliferation caused by hyaluronic acid was attenuated completely by the anti-CD44 mAbs, 212.3 and IM7.8.1. Pretreatment of CD34(+) cells with 5 mu g/ml 212.3 inhibited the augmented proliferation caused by the optimal concentration of hyaluronic acid (100 mu g/ml) from 260 +/- 39.2% of control growth to 114 +/- 16.4% of control growth ($p = 0.02$). Inhibition was comparable for IM7.8.1. Control mAb (LM2) to the beta(2) integrin subunit CD11b had no effect on proliferation induced by hyaluronic acid. We demonstrate that hyaluronic acid stimulates the growth of CD34(+) selected umbilical cord blood cells into specifically differentiated mature eosinophils. This process is modulated by the CD44 receptor on the progenitor cell population.

7/3,AB/163 (Item 44 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci

03751407 Genuine Article#: QC782 Number of References: 52 Title: EXPRESSION OF PROTEOGLYCANS AND *HYALURONAN* DURING WOUND-HEALING (Abstract Available)
Author(s): OKSALA O; SALO T; TAMMI R; HAKKINEN L; JALKANEN M; INKI P; LARJAVA H
Corporate Source: UNIV BRITISH COLUMBIA,DEPT CLIN DENT SCI,DIV PERIODONT,2199 WESBROOK MALL/VANCOUVER/BC V6T 1Z3/CANADA/; UNIV BRITISH COLUMBIA,DEPT CLIN DENT SCI,DIV PERIODONT/VANCOUVER/BC V6T 1Z3/CANADA/; UNIV TURKU,DEPT PERIODONTOL/TURKU//FINLAND/; UNIV TURKU,DEPT ORAL BIOL/TURKU//FINLAND/; UNIV TURKU,INST DENT/TURKU//FINLAND/; UNIV OULU,DEPT ORAL SURG & PATHOL/OULU//FINLAND/; UNIV KUOPIO,DEPT ANAT/KUOPIO//FINLAND/; CTR BIOTECHNOL/TURKU//FINLAND/; UNIV BRITISH COLUMBIA,DEPT CLIN DENT SCI/VANCOUVER/BC/CANADA/
Journal: JOURNAL OF HISTOCHEMISTRY & CYTOCHEMISTRY, 1995, V43, N2 (FEB), P 125-135 ISSN: 0022-1554
Language: ENGLISH Document Type: ARTICLE
Abstract: We investigated the expression of proteoglycans (PGs) and hyaluronan (HA) during healing of human mucosal wounds, Biopsy specimens of experimental wounds were taken 1, 3, and 7 days after wounding, Frozen sections were used for immunolocalization of CD44, syndecan-1, basement membrane-associated heparan sulfate proteoglycan (BM-HSPG), decorin, and biglycan, HA was localized in paraffin sections with a specific HA-binding probe, Epithelium showed first signs of migration on Day 1, more progressive migration on Day 3, and epithelial sheets confronted on Day 7, CD44 surrounded migrating keratinocytes at all stages of wound healing, In epithelium, CD44 and HA remarkably localized to the same region, Expression of syndecan-1 was switched from the suprabasal cell layer of unwounded epithelium to the basal cell layer of the migrating wound epithelium, BM-HSPG was absent under migrating keratinocytes. It started to reappear at the basement membrane zone on Day 7, The area under the wound epithelium containing newly synthesized collagen fibers first became positive for decorin on Day 7, whereas staining of biglycan was negative. Granulation tissue was also strongly positive for CD44 and hyaluronan, Our results indicate that migrating keratinocytes express both CD44 and syndecan-1 but not BM-HSPG, During differentiation of keratinocytes, expression of CD44 preceded that of syndecan-1, The results suggest that different HSPGs have multiple functions in keratinocyte migration and differentiation during reepithelialization.

7/3,AB/164 (Item 45 from file: 34)
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03734479 Genuine Article#: QB808 Number of References: 34 Title: *HYALURONAN* ON THE SURFACE OF TUMOR-CELLS IS CORRELATED WITH METASTATIC BEHAVIOR (Abstract Available)
Author(s): ZHANG LR; UNDERHILL CB; CHEN LP
Corporate Source: GEORGETOWN UNIV,MED CTR,VINCENT T LOMBARDI CANCRES CTR,DEPT CELL BIOL,3800 RESERVOIR RD/WASHINGTON//DC/20007; BRISTOL MYERS SQUIBB PHARMACEUT RES INST/SEATTLE//WA/98121
Journal: CANCER RESEARCH, 1995, V55, N2 (JAN 15), P428-433 ISSN: 0008-5472
Language: ENGLISH Document Type: ARTICLE
Abstract: In the present study, we examined the metastatic potential of tumor cells expressing different levels of cell surface hyaluronan. We used flow cytometry to isolate subsets of the B16-F1 mouse melanoma cell line that expressed either high (HA-H) or low (RA-L) amounts of hyaluronan on their surfaces. These two subsets of cells showed a 32-fold difference in the amount of cell surface hyaluronan, due to its rate of synthesis. However, these cell Lines did not differ from each other with regard to their in vitro growth rates, susceptibility to natural killer-mediated cytotoxicity, or the expression of the cell surface proteins CD44, ICAM-1, and GMP-140. When these cells were injected s.c., they both formed s.c. tumors of approximately the same size. However, when injected into the tail vein of mice, the HA-H cells formed a greater number of nodules in the lungs and caused a faster rate of mortality than the HA-L cells. The presence of hyaluronan did enhance the interaction of the HA-H cells with cultured endothelial cells that expressed CD44. Thus, it is possible that enhanced interactions between hyaluronan and CD44 promoted the formation of tumor embolisms which, in turn, increased the chances that the tumor cells would be trapped in the lungs. Taken together, these results suggest that hyaluronan may play a critical role in the process of tumor metastasis.

7/3,AB/165 (Item 46 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci
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03717977 Genuine Article#: BB89M Number of References: 366 Title: *HYALURONAN* METABOLISM IN SKIN - INTRODUCTION
Author(s): TAMMI R; AGREN UM; TUHKANEN AL; TAMMI M
Corporate Source: UNIV KUOPIO,DEPT ANAT,POB 1627/SF-70211 KUOPIO//FINLAND/ Journal: PROGRESS IN HISTOCHEMISTRY AND CYTOCHEMISTRY, 1994, V29, N2, P1-77 ISSN: 0079-6336
Language: ENGLISH Document Type: REVIEW

7/3,AB/166 (Item 47 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci
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03704403 Genuine Article#: PZ446 Number of References: 36 Title: ADHESION MOLECULES ON INTERMEDIATE TCR CELLS .1. UNIQUE EXPRESSION OF ADHESION MOLECULES, CD44(+) L-SELECTIN(-), ON INTERMEDIATE TCR CELLS IN THE LIVER AND THE MODULATION OF THEIR ADHESION BY *HYALURONIC* -ACID (Abstract Available)
Author(s): ARAI K; IIAI T; NAKAYAMA M; HASEGAWA K; SATO K; OHTSUKA K; WATANABE H; HANYU T; TAKAHASHI HE; ABO T
Corporate Source: NIIGATA UNIV,SCH MED,DEPT IMMUNOL,ASAHIMACHI DORI 1/NIIGATA 951//JAPAN/; NIIGATA UNIV,SCH MED,DEPT IMMUNOL/NIIGATA 951//JAPAN/; NIIGATA UNIV,SCH MED,DEPT ORTHOPED/NIIGATA//JAPAN/
Journal: IMMUNOLOGY, 1995, V84, N1 (JAN), P64-71 ISSN: 0019-2805
Language: ENGLISH Document Type: ARTICLE
Abstract: In addition to thymus-derived T cells, it was demonstrated recently that extrathymically differentiated T cells exist in the liver and other immune organs of mice. Since such extrathymic T cells have T-cell receptors (TCR) of intermediate intensity (i.e. intermediate TCR cells) and constitutively express IL 2 receptor beta-chain (IL-2R beta) similar to natural killer (NK) cells, they are easily distinguished from thymus-derived T cells with a TCR-bright(+) IL-2R beta(-) phenotype (i.e. bright TCR cells). In the present study, the expression of adhesion molecules CD44 and L-selectin was compared between these T-cell subsets. Intermediate TCR cells in the liver and other organs were found to be CD44(+) L-selectin(-) and, inversely, bright TCR cells were CD44(-) L-selectin(+). CD3(-) IL-2R beta(+) NK cells were also estimated to be CD44(+) L-selectin(-). Hyaluronic acid, which is known to adhere to a CD44 ligand, bound to intermediate TCR cells, but not to bright TCR cells. Among many extracellular matrices, hyaluronic acid induced a prominent decrease in the numbers and proportions of intermediate TCR cells and NK cells in the liver from 6 to 24 hr after in vivo administration. The half-life span of injected hyaluronic acid was approximately 7 hr in the plasma. These results suggest that the CD44 molecule, which is uniquely expressed on intermediate TCR cells and NK cells, is eventually associated with their adhesion to the sinusoidal walls in the liver.

7/3,AB/167 (Item 48 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci
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03666274 Genuine Article#: PV959 Number of References: 54 Title: EPICAN, A HEPARAN *CHONDROITIN* SULFATE PROTEOGLYCAN FORM OF CD44, MEDIATES CELL-CELL ADHESION (Abstract Available) Author(s): MILSTONE LM; HOUGHMONROE L; KUGELMAN LC; BENDER JR; HAGGERTY JG Corporate Source: VET AFFAIRS MED CTR,DERMATOL SERV/W HAVEN//CT/06516; YALE UNIV,SCH MED,DEPT DERMATOL/NEW HAVEN//CT/06510; YALE UNIV,SCH MED,DEPT INTERNAL MED/NEW HAVEN//CT/06510 Journal: JOURNAL OF CELL SCIENCE, 1994, V107, NOV (NOV), P3183-3190 ISSN: 0021-9533
Language: ENGLISH Document Type: ARTICLE
Abstract: Epican is a heparan/chondroitin sulfate proteoglycan form of CD44 and is expressed on the surface of keratinocytes from the basal layer to the granular layer of the epidermis. To analyze the adhesive properties of epican apart from the influence of other adhesive molecules found on keratinocytes, mouse L cell fibroblasts were transfected with CD44Epican cDNA. The epican expressed on the surface of transfected L cells was predominantly a heparan or chondroitin sulfate proteoglycan.

The CD44Epican-transfected L cells acquired: (a) a self-aggregating phenotype that required hyaluronan but was calcium-independent; and (b) a new capacity to adhere to keratinocytes, a property that was blocked by an anti-epican antibody. Both aggregation and adhesion of CD44Epican-transfected cells were completely prevented by pretreatment with hyaluronidase, but were totally restored by the addition of exogenous hyaluronan, Aggregation of transfected L cells was minimally influenced by other glycosaminoglycans, but adhesion of transfected L cells to keratinocytes was substantially inhibited by heparin.

The ability of epican to mediate adhesion between keratinocytes was evaluated in a newly developed adhesion assay, In the presence of 0.03 mM calcium, a monoclonal antibody against epican inhibited keratinocyte adhesion to keratinocyte monolayers by 80%.

These data demonstrate that epican causes adhesion and aggregation in the transfected L cell model system, that the adhesive function of epican is hyaluronan-dependent, and that epican could have an adhesive function in intact epidermis.

7/3,AB/168 (Item 49 from file: 34)
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03643564 Genuine Article#: PU277 Number of References: 23 Title: SYNTHESIS OF *HYALURONIC*-ACID RELATED DI-SACCHARIDES AND TETRA-SACCHARIDES HAVING A GLUCURONIC-ACID AT THE REDUCING END (Abstract Available)
Author(s): SLAGHEK TM; HYPPONEN TK; OGAWA T; KAMERLING JP; VLIEGENTHART JFG Corporate Source: UNIV UTRECHT,BIJVOET CTR,DEPT BIOORGAN CHEM,POB80075/3508 TB UTRECHT//NETHERLANDS/; UNIV UTRECHT,BIJVOET CTR,DEPT BIOORGAN CHEM/3508 TB UTRECHT//NETHERLANDS/; RIKEN,INST PHYS & CHEM RES/WAKO/SAITAMA 35101/JAPAN/
Journal: TETRAHEDRON-ASYMMETRY, 1994, V5, N11 (NOV), P2291-2301 ISSN: 0957-4166
Language: ENGLISH Document Type: ARTICLE
Abstract: The synthesis is reported of 4-methoxyphenyl

O-(2-acetamido-2-deoxy-beta-D-glucopyranosyl)-(1-->4)-beta-D-glucopyran osyluronic acid (1) and 4-methoxyphenyl

O-2-acetamido-2-deoxy-beta-D-glucopyranosyl)-(1-->4)-O-(beta-D-glucopyr anosyluronic

acid)-(1-->3)-O-(2-acetamido-2-deoxy-beta-D-glucopyranosyl)- (1-->4-beta-D-glucopyranosyluronic acid (5), which represent structural elements of hyaluronic acid.

3,4,6-Tri-O-acetyl-2-deoxy-2-phthalimido-beta-D-glucopyranosyl trichloroacetimidate (3) was condensed with 4-methoxyphenyl 6-O-levulinoyl-2,3-di-O-p-toluoyl-beta-D-glucopyranoside (4) in dichloromethane, using boron trifluoride etherate as a promoter, yielding 4-methoxyphenyl O-(3,4,6-tri-O-acetyl-2-deoxy-2-phthalimido-beta-D-

glucopyranosylyl)-(1-->4)6-O-levulinoyl-2,3-di-O-p-toluoyl-beta-D-gluco pyranoside (2). Subsequent delevulinoylation, oxidation, complete deprotection, and N-acetylation gave 1. Coupling of

3-O-allyloxycarbonyl-2-deoxy-4,6-O-isopropylidene-2-phthalimido- beta-D-glucopyranosyl trichloroacetimidate (9) with 4, followed by de-allyloxycarbonylation of the obtained disaccharide derivative gave 4-methoxyphenyl O-(2-deoxy-4,6-O-isopropylidene-2-phthalimido-beta-D-

glucopyranosyl)-(1-->4)-6-O-levulinoyl-2,3-di-O-p-toloyl-beta-D-glucopy ranoside (8). Demethoxyphenylation and subsequent imidation of 2 afforded O-(3,4,6-tri-O-acetyl-2-deoxy-2-phthalimido-beta-D-glucopyranosyl)-(1-->4)-6-O-levulinoyl-2,3-di-O-p-toluoyl-a

lpha/beta-D- glucopyranosylucopyranosyl trichloroacetimidate (7). Condensation of 7 and 8 in dichloromethane, with trimethylsilyl trifluoromethanesulfonate as a promoter, gave tetrasaccharide derivative 15. Subsequent de-isopropylidenation, O-acetylation, delevulinoylation, oxidation, complete deprotection, and N-acetylation yielded 5.

7/3,AB/169 (Item 50 from file: 34)
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03596978 Genuine Article#: PQ184 Number of References: 7 Title: CD44 MEDIATES *HYALURONAN*-BINDING BY HUMAN MYELOID KG1A AND KG1 CELLS (Abstract Available)
Author(s): MORIMOTO K; ROBIN E; LI Y; LEGRAS S; LEBOUSSEKERDILES MC; CLAY D ; JASMIN C; SMADJAJOFFE F
Corporate Source: HOP PAUL BROUSSE,INSERM,U268,UNITE ONCOGENESE APPL,14 AVE PAUL VAILLANT COUTURIER/F-94800 VILLEJUIF//FRANCE/; HOP PAUL BROUSSE,INSERM,U268,UNITE ONCOGENESE APPL/F-94800 VILLEJUIF//FRANCE/ Journal: BULLETIN DU CANCER, 1994, V81, N11 (NOV), P949-951 ISSN: 0007-4551
Language: FRENCH Document Type: ARTICLE
Abstract: Hyaluronan-binding function of the CD44 molecule has not been so far detected in myeloid cells. In order to study pure populations of primitive myeloid cells, we investigated the hyaluronan-binding function of the CD44 molecule from three myeloid cell lines: KG1a KG1 and HMO. Both KG1a and KG1 cells express the CD34 antigen characteristic of the hematopoietic stem cells, and HL60 cells do not; accordingly, KG1a and KG1 cells are generally considered as the most primitive, and HL60 cells as the mast mature of these cell lines. Measurement of cell adhesion to hyaluronan-coated surfaces, using Cr-51-labeled cells, and of aggregate formation in
hyaluronan-containing solutions, showed that 45% of KG1 cells and 22-24% of KG1a spontaneously bind to hya[uronan whereas HMO cells do not, either spontaneously or after treatment with a phorbol ester. Hyaluronan binding by KG1a and KG1 cells is mediated by CD44, because if is specifically abolished by monoclonal antibodies to this molecule. The binding might require phosphorylation by protein kinase C, and perhaps also by protein kinase A, because it is prevented by staurosporine, that inhibits these enzymes. TPA, that activates protein kinase C, rises to 80% the proportion of KG1 and KG1a cells which bind hyaluronan; this activation is dependent on protein synthesis for it is abrogated by cyclophosphamide, a protein synthesis inhibitor. Binding of TPA-treated cells to hyaluronan is only partly inhibited by monoclonal antibody to CD44: this suggests that TPA may induce synthesis of a hyaluronan-binding protein distinct from CD44. Considering the abundance of hyaluronan in human bone-marrow, these results suggest that CD44 may be involved in mediating precursor-stroma interaction.

7/3,AB/170 (Item 51 from file: 34)
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03511395 Genuine Article#: PJ472 Number of References: 36 Title: THE FORMATION OF HUMAN SYNOVIAL JOINT CAVITIES - A POSSIBLE ROLE FOR *HYALURONAN* AND CD44 IN ALTERED INTERZONE COHESION (Abstract Available)
Author(s): EDWARDS JCW; WILKINSON LS; JONES HM; SOOTHILL P; HENDERSON KJ; WORRALL JG; PITSILLIDES AA
Corporate Source: UNIV COLL & MIDDLESEX SCH MED,DEPT RHEUMATOL,TOTTENHAM ST/LONDON W1P 9PG//ENGLAND/; UNIV COLL & MIDDLESEX SCH MED,DEPT HAEMATOL/LONDON WC1E 6HX//ENGLAND/; UNIV COLL & MIDDLESEX SCH MED,DEPT OBSTET & GYNECOL/LONDON//ENGLAND/; INST CHILD HLTH/LONDON//ENGLAND/ Journal: JOURNAL OF ANATOMY, 1994, V185, OCT (OCT), P355-367 ISSN: 0021-8782
Language: ENGLISH Document Type: ARTICLE
Abstract: During fetal development, cavitation occurs within the primitive skeleton along planes destined to become the articular surfaces of synovial joints. A histochemical study of human fetal limbs was undertaken to identify the cell types involved in this cavitation. and the possible role of interactions between cells and extracellular matrix. Cryostat sections were stained with antibodies to CD68, factor VIII related antigen, prolyl hydroxylase, beta 1 integrin, VCAM-1, proliferating cell nuclear antigen, chondroitin-4 sulphate, chondroitin-6-sulphate, hyaluronan synthase and CD44. Similar sections were reacted for uridine diphosphoglucose dehydrogenase (UDPGD) and acid phosphatase activity. Hyaluronan was demonstrated using an aggrecan core protein hyaluronan binding region probe. Macrophages were present prior to cavitation in the periphery of joint interzones but not at the presumptive joint line in the central interzone. Fibroblastic cells were present throughout. Absence of local VCAM-1 expression indicated that cavitation was temporally distinct from full
fibroblast-like synoviocyte differentiation. CD44 was expressed by interzone cells at all stages. Staining for

hyaluronan and hyaluronan synthase, but not chondroitin sulphates was present in the interzone before and at the time of cavitation. UDPGD activity was increased in a narrow band of cells at the presumptive joint line prior to cavitation. These findings suggest that joint cavitation is dependent on the behaviour of fibroblastic cells and/or adjacent chondrocytes, rather than macrophages. Since UDPGD activity is involved in hyaluronan synthesis, it is proposed that joint cavitation is facilitated by a rise in local hyaluronan concentration in an area of tissue where cohesion is dependent on the interaction between cellular CD44 and extracellular hyaluronan. As proposed by Toole et al. (1984) such a local rise in hyaluronan concentration may lead to a switch from intercellular cohesion to dissociation, leading to tissue cavitation.

7/3,AB/171 (Item 52 from file: 34)
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03374664 Genuine Article#: PB318 Number of References: 69 Title: ANKYRIN-BINDING DOMAIN OF CD44(GP85) IS REQUIRED FOR THE EXPRESSION OF *HYALURONIC* ACID-MEDIATED ADHESION FUNCTION (Abstract Available)
Author(s): LOKESHWAR VB; FREGIEN N; BOURGUIGNON LYW
Corporate Source: UNIV MIAMI,SCH MED,DEPT CELL BIOL & ANAT R124,1600 NW 10TH AVE/MIAMI//FL/33101; UNIV MIAMI,SCH MED,DEPT CELL BIOL & ANAT R124/MIAMI//FL/33101
Journal: JOURNAL OF CELL BIOLOGY, 1994, V126, N4 (AUG), P1099-1109 ISSN: 0021-9525
Language: ENGLISH Document Type: ARTICLE
Abstract: GP85 is one of the most common hemopoietic isoforms of the cell adhesion molecule, CD44. CD44(GP85) is known to contain at least one ankyrin-binding site within its 70 aa cytoplasmic domain and to bind hyaluronic acid (HA) with its extracellular domain. In this study we have mapped the ankyrin-binding domain of CD44(GP85) by deleting various portions of the cytoplasmic region followed by expression of these truncated cDNAs in COS cells. The results of these experiments indicate that the ankyrin-binding domain resides between amino acids 305 and 355. Biochemical analyses, using competition binding assays and a synthetic peptide (NGGNGTVEDRKPSEL) containing 15 aa between aa 305 and aa 320, support the conclusion that this region is required for ankryin binding. Furthermore, we have constructed a fusion protein in which this 15 aa sequence of CD44(GP85) is transplanted onto another transmembrane protein which does not bind ankyrin. Our results show that this fusion protein acquires the ability to bind ankyrin confirming that the sequence ((306)NGGNGTVEDRKPSE(320)L) is a critical part of the ankryin-binding domain of CD44(GP85). In addition, we have demonstrated that deletion of this 15 aa ankyrin-binding sequence from CD44(GP85) results in a drastic reduction (greater than or equal to 90%) of HA-binding and HA-mediated cell adhesion. These findings strongly suggest that ankyrin binding to the cytoplasmic domain of CD44(GP85) plays a pivotal role in regulating hyaluronic acid-mediated cell-cell and cell-extracellular matrix interactions.

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03365490 Genuine Article#: NZ738 Number of References: 34 Title: BINDING AND DEGRADATION OF *HYALURONAN* BY HUMAN BREAST-CANCER CELL-LINES EXPRESSING DIFFERENT FORMS OF CD44 - CORRELATION WITH INVASIVE POTENTIAL (Abstract Available)
Author(s): CULTY M; SHIZARI M; THOMPSON EW; UNDERHILL CB
Corporate Source: GEORGETOWN UNIV,MED CTR,DEPT CELL BIOL/WASHINGTON//DC/20007; GEORGETOWN UNIV,MED CTR,VINCENT T LOMBARDI CANCRES CTR/WASHINGTON//DC/20007
Journal: JOURNAL OF CELLULAR PHYSIOLOGY, 1994, V160, N2 (AUG), P275-286 ISSN: 0021-9541
Language: ENGLISH Document Type: ARTICLE
Abstract: In the present study, we examined a panel of human breast cancer cell lines with regard to their expression of CD44 and ability to bind and degrade hyaluronan. The cell lines expressed varying amounts of different molecular weight forms of CD44 (85-200 kDa) and, in general, those that expressed the greatest amounts of CD44 were the most invasive as judged by in vitro assays. In addition, the ability to bind and degrade hyaluronan was restricted to the cell lines expressing high levels of CD44, and both these functions were blocked by an antibody to CD44 (Hermes-1). Moreover, the rate of [H-3]hyaluronan degradation was highly correlated with the amount of CD44 ($r = 0.951$, $P < 0.0001$), as well as with the invasive potential of the cells. Scatchard analysis of the [H-3]hyaluronan binding of these cells revealed the existence of significant differences in both their binding capacity and their dissociation constant. To determine the source of this deviation, the different molecular weight forms of CD44 were partially separated by gel filtration chromatography. In all cell lines, the 85 kDa form was able to bind hyaluronan, although with different affinities. In contrast, not all of the high molecular weight forms of CD44 had this ability. These

results illustrate the diversity of CD44 molecules in invasive tumor cells, and suggest that one of their major functions is to degrade hyaluronan. (C) 1994 Wiley-Liss, Inc.

7/3,AB/173 (Item 54 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci
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03332851 Genuine Article#: NZ252 Number of References: 109 Title: ISOLATION OF A NEURAL *CHONDROITIN* SULFATE PROTEOGLYCAN WITH NEURITE OUTGROWTH-PROMOTING PROPERTIES (Abstract Available) Author(s): FAISSNER A; CLEMENT A; LOCHTER A; STREIT A; MANDL C; SCHACHNER M Corporate Source: UNIV HEIDELBERG,DEPT NEUROBIOL,NEUENHEIMER FELD364/D-69120 HEIDELBERG//GERMANY/; ETH ZURICH,DEPT NEUROBIOL/CH-8093 ZURICH//SWITZERLAND/ Journal: JOURNAL OF CELL BIOLOGY, 1994, V126, N3 (AUG), P783-799 ISSN: 0021-9525
Language: ENGLISH Document Type: REVIEW
Abstract: Proteoglycans are expressed in various tissues on cell surfaces and in the extracellular matrix and display substantial heterogeneity of both protein and carbohydrate constituents. The functions of individual proteoglycans of the nervous system are not well characterized, partly because specific reagents which would permit their isolation are missing. We report here that the monoclonal antibody 473HD, which binds to the surface of early differentiation stages of murine astrocytes and oligodendrocytes, reacts with the chondroitin sulfate/dermatan sulfate hybrid epitope DSD-1 expressed on a central nervous system chondroitin sulfate proteoglycan designated DSD-1-PG. When purified from detergent-free postnatal days 7 to 14 mouse brain extracts, DSD-1-PG displays an apparent molecular mass between 800-1,000 kD with a prominent core glycoprotein of 350-400 kD. Polyclonal anti-DSD-1-PG antibodies and monoclonal antibody 473HD react with the same molecular species as shown by immunocytochemistry and sequential immunoprecipitation performed on postnatal mouse cerebellar cultures, suggesting that the DSD-1 epitope is restricted to one proteoglycan. DSD-1-PG promotes neurite outgrowth of embryonic day 14 mesencephalic and embryonic day 18 hippocampal neurons from rat, a process which can be blocked by monoclonal antibody 473HD and by enzymatic removal of the DSD-1-epitope. These results show that the hybrid glycosaminoglycan structure DSD-1 supports the morphological differentiation of central nervous system neurons.

7/3,AB/174 (Item 55 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci
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03092249 Genuine Article#: NB873 Number of References: 27 Title: SYNTHESIS OF OLIGOSACCHARIDES RELATED TO *HYALURONIC*-ACID .2. SYNTHESIS OF *HYALURONIC* ACID-RELATED DI-SACCHARIDES, TRI-SACCHARIDES, AND TETRA-SACCHARIDES HAVING AN N-ACETYLGLUCOSAMINE RESIDUE AT THE REDUCING END (Abstract Available)
Author(s): SLAGHEK TM; NAKAHARA Y; OGAWA T; KAMERLING JP; VLIEGENTHART JFG Corporate Source: UNIV UTRECHT,BIJVOET CTR,DEPT BIOORGAN CHEM,POB80075/3508 TB UTRECHT//NETHERLANDS/; RIKEN,INST PHYS & CHEM RES/WAKO/SAITAMA 35101/JAPAN/; UNIV TOKYO,FAC AGR,BUNKYO KU/TOKYO 113//JAPAN/
Journal: CARBOHYDRATE RESEARCH, 1994, V255, MAR (MAR 4), P61-85 ISSN: 0008-6215
Language: ENGLISH Document Type: ARTICLE
Abstract: The synthesis is reported of 4-methoxyphenyl O-(beta-D-glucopyranosyluronic acid)-(1 --> 3)-2-acetamido-2-deoxy-beta-D-glucopyranoside (1), 4-methoxyphenyl O-(2-acetamido-2-deoxy-beta-D-glucopyranosyl)-(1 --> 4)-O-(beta-D-glucopyranosyluronic acid)-(1 --> 3)-2-acetamido-2-deoxy-beta-D-glucopyranoside (5), and 4-methoxyphenyl O-(beta-D-glucopyranosyluronic acid)-(1 --> 3)-O-(2-acetamido-2-deoxy-beta-D-glucopyranosyl)-(1 --> 4)-O-(beta-D-glucopyranosyluronic acid)-(1 --> 3)-2-acetamido-2-deoxy-beta-D-glucopyranoside (10), which are structural elements of the extracellular polysaccharide hyaluronic acid. 6-O-Levulinoyl-2,3,4-tri-O-p-toluoyl-alpha-D-glucopyranosyl trichloroacetimidate (3) was condensed with 4-methoxyphenyl 2-deoxy-4,6-O-isopropylidene-2-phthalimido-beta-D-glucopyranoside (4). De-isopropylidenation and acetylation of the obtained disaccharide derivative yielded 4-methoxyphenyl

O-(6-O-levulinoyl-2,3,4-tri-O-p-toluoyl-beta-D-glucopyranosyl)-(1 --> 3)-4,6-di-O-acetyl-2-deoxy-2-phthalimido-beta-D-glucopyranoside, and subsequent delevulinoylation, oxidation, complete deprotection, and N-acetylation gave 1. Coupling of

4-O-allyloxycarbonyl-6-O-levulinoyl-2,3-di-O-p-toluoyl-alpha-D-glucopyr anosyl trichloroacetimidate with 4 followed by de-isopyropylidenation, acetylation, and deallyloxycarbonylation of the obtained disaccharide derivative gave 8. Condensation of

3,4,6-tri-O-acetyl-2-deoxy-2-phthalimido-beta-D-glucopy ranosyl trichloroacetimidate with 8 afforded trisaccharide derivative 4-methoxyphenyl

O-(3,4,6-tri-O-acetyl-2-deoxy-2-phthalimido-beta-D-gluc opyranosyl-(1 -->
4)-O-(6-O-levulinoyl-2,3-di-O-p-toluoyl-beta-D-glucopyran osyl)-(1 -->
3)-4,6-di-O-acetyl-2-deoxy-2-phthalimido-beta-D-glucopy ranoside, and subsequent delevulinoylation, oxidation, complete deprotection, and N-acetylation gave 5.

3-O-Allyloxycarbonyl-2-deoxy-4,6-O-isopropylidene-2-pht halimido-beta-D- glucopyranosyl trichloroacetimidate was coupled with disaccharide acceptor 8, and deallyloxycarbonylation of the obtained trisaccharide derivative yielded 12. Condensation of 3 with 12 followed by de-isopropylidenation and acetylation of the obtained tetrasaccharide derivative gave 4-methoxyphenyl

O-(6-O-levulinoyl-2,3,4-tri-O-p-toluoyl-beta-D-glucopyran osyl)-(1 -->
3)-O-(4,6-di-O-acetyl-2-deoxy-2-phthalimido-beta-D-gluc opyranosyl)-(1 -->
4)-O-(6-O-levulinoyl-2,3-di-O-p-toluoyl-beta-D-glucopyran osyl)-(1 -->
3)-4,6-di-O-acetyl-2-deoxy-2-phthalimido-beta-D-glucopy ranoside, and delevulinoylation, oxidation, complete deprotection, and N-acetylation yielded 10.

7/3,AB/175 (Item 56 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci
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03034351 Genuine Article#: NB411 Number of References: 39 Title: LIGAND-BINDING SPECIFICITY OF ALTERNATIVELY SPLICED CD44 ISOFORMS - RECOGNITION AND BINDING OF *HYALURONAN* BY CD44R1 (Abstract Available)
Author(s): DOUGHERTY GJ; COOPER DL; MEMORY JF; CHIU RK
Corporate Source: BRITISH COLUMBIA CANC RES CTR,TERRY FOX LAB,TUMOUR IMMUNOL GRP,601 W 10TH AVE/VANCOUVER V5Z 1L3/BC/CANADA/; BRITISH COLUMBIA CANC AGCY,TERRY FOX LAB HEMATOL ONCOL/VANCOUVER V5Z 1L3/BC/CANADA/; UNIV BRITISH COLUMBIA,DEPT PATHOL/VANCOUVER/BC/CANADA/; UNIV PITTSBURGH,DEPT PATHOL/PITTSBURGH//PA/15281
Journal: JOURNAL OF BIOLOGICAL CHEMISTRY, 1994, V269, N12 (MAR 25), P 9074-9078
ISSN: 0021-9258
Language: ENGLISH Document Type: ARTICLE

Abstract: CD44 species of widely differing molecular mass have been identified on various normal and/or transformed cells. Recent studies have demonstrated that much of this heterogeneity is produced as a result of the alternative splicing of a series of 10 exons present within the CD44 gene generating a large number of CD44 isoforms containing additional peptide sequences of varying length inserted into a single site within the extracellular domain of the molecule. At present, the effect of such insertions on the ligand binding specificity of CD44 re mains unclear. CD44H, the major CD44 isoform expressed by most resting cell types, has been shown to function as a receptor for the glycosaminoglycan hyaluronan. In contrast, CD44E, the major isoform expressed by the colon carcinoma cell line HT29, which contains a 132-amino acid insert, is unable to recognize and bind this ligand. In the present study we demonstrate that CD44R1, an isoform isolated from the myelomonocytic cell line KG1a, that differs from CD44E by just 3 amino acid substitutions, is fully capable of mediating the attachment of transfected COS7 cells to hyaluronancoated plastic. In order to confirm that such binding was directly mediated by the introduced CD44 species, chimeric proteins containing the entire extracellular domain of CD44H or CD44R1 fused in-frame to human bone/liver/kidney alkaline phosphatase were prepared and tested for their ability to bind hyaluronan-coated plastic. Both fusion proteins bound equally well to hyaluronan and in each case their attachment could be readily inhibited by monoclonal antibodies directed against the hyaluronan-binding domain of CD44. These data indicate that the 132-amino acid insert present within the extracellular domain of CD44R1 does not interfere with the hyaluronan binding function of the molecule. Since CD44E contains an identically sized insert but is unable to bind hyaluronan, it is likely that mutation of one or more of the 3 amino acid residues that differ between CD44E and CD44R1 is responsible for the altered functional activity of this particular molecule.

7/3,AB/176 (Item 57 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci
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02978610 Genuine Article#: MU439 Number of References: 35 Title: CHANGES IN *HYALURONAN* DEPOSITION DURING EARLY RESPIRATORY-DISTRESS SYNDROME IN PREMATURE MONKEYS (Abstract Available)
Author(s): JUUL SE; KINSELLA MG; JACKSON JC; TRUOG WE; STANDAERT TA; HODSON WA
Corporate Source: JHMHC,DEPT PEDIAT,DIV NEONATOL,BOX 100296/GAINESVILLE//FL/32610; UNIV

WASHINGTON,DEPT PEDIAT/SEATTLE//WA/98195; UNIV WASHINGTON,DEPT PATHOL/SEATTLE//WA/98195 ; UNIV FLORIDA,DEPT PEDIAT/GAINESVILLE//FL/32606
Journal: PEDIATRIC RESEARCH, 1994, V35, N2 (FEB), P238-243 ISSN: 0031-3998
Language: ENGLISH Document Type: ARTICLE
Abstract: Increased deposition of hyaluronan (HA) is part of the early response to fibrogenic stimulus in the lung exposed to bleomycin injury and has been associated with increased lung water in adult animals. Early respiratory distress syndrome (RDS) in premature infants is characterized by increased lung water, and late sequelae include fibrosis or bronchopulmonary dysplasia. We hypothesized that increased HA in the alveolar interstitium would be associated with increasingly severe RDS in prematurely delivered monkeys and that modes of therapy that affect severity of disease such as treatment with high-frequency oscillatory ventilation or exogenous surfactant would decrease this response. Thirty-four Macaca nemestrina monkeys were delivered at 134 +/- 1 d (term = 168 d) and randomized to high-frequency oscillatory ventilation or conventional mechanical ventilation from birth. Sixteen of these animals received surfactant. At 6 h of age, the right lower lung was frozen in situ during inflation to 30 cm H2O (approximately 2940 Pa) and then dehydrated and processed for microscopy. The presence and severity of RDS were evaluated by clinical and morphologic criteria. HA concentrations in lung extracts increased with progressively severe RDS (p = 0.0003). Treatment with high-frequency oscillatory ventilation decreased the lung injury score (1.69 +/- 0.7 compared with 2.5 +/- 0.9, p = 0.05), but changes in lung HA concentration did not reach significance (37.9 +/- 22.7 compared with 44.8 +/- 22.6). Surfactant treatment decreased lung HA concentration (29.6 +/- 19.0 mu g/wet lung) compared with non-surfactant-treated animals (54.7 +/- 20.2 mu g/g wet lung, p = 0.0009). Two fetal animals (144 and 163 d gestation) and seven additional premature animals ventilated for up to 96 h were compared with the animals killed at 6 h. HA concentrations increased with length of mechanical ventilation and severity of illness in these animals. HA was localized in freeze-dried lung sections using a biotinylated probe. Lung sections were blindly scored for the distribution of HA staining, and these scores were positively correlated with HA concentration measurements (r = 0.75, p < 0.0001). The quantity of HA in alveolar microvasculature correlated with severity of RDS (r = 0.68, p = 0.0004). We conclude that 1) HA concentration in RDS lungs of prematurely delivered infant monkeys is increased relative to normal lungs at 6 h, 2) increased HA is localized predominantly to the perivascular space of lung vasculature, and 3) this response is decreased by surfactant treatment.

7/3,AB/177 (Item 58 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci
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02978031 Genuine Article#: MV412 Number of References: 0 Title: NEOINTIMAL FORMATION FOLLOWING BALLOON CATHETER INJURY - THE ROLE OF *HYALURONAN* (*HA*) AND THE *HA* *RECEPTOR* RHAMM Author(s): SAVANI RC; WANG C; SHI YF; KAPLAN C; PANEK R; STERN R; TURLEY EA
Corporate Source: DEPT PEDIAT/WINNIPEG/MB/CANADA/; MANITOBA INST CELL BIOL/WINNIPEG/MB/CANADA/; PARKE DAVIS RES DEV/ANN ARBOR//MI/00000; UCSF,DEPT PATHOL/SAN FRANCISCO//CA/00000
Journal: JOURNAL OF CELLULAR BIOCHEMISTRY, 1994, S18A (JAN 4), P321 ISSN: 0730-2312
Language: ENGLISH Document Type: MEETING ABSTRACT

7/3,AB/178 (Item 59 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci
(c) 2002 Inst for Sci Info. All rts. reserv.

02977867 Genuine Article#: MV412 Number of References: 0 Title: THE EXPRESSION OF *HYALURONAN* (*HA*) AND THE *HA* *RECEPTOR*, RHAMM, IN EXPERIMENTAL MYOCARDIAL-INFARCTION Author(s): SAVANI RC; WANG C; STERN R; TURLEY EA
Corporate Source: DEPT PEDIAT/WINNIPEG R3E 0V9/MB/CANADA/; MANITOBA INST CELL BIOL/WINNIPEG R3E 0V9/MB/CANADA/; UNIV CALIF SAN FRANCISCO,DEPT PATHOL/SAN FRANCISCO//CA/00000
Journal: JOURNAL OF CELLULAR BIOCHEMISTRY, 1994, S18A (JAN 4), P273 ISSN: 0730-2312
Language: ENGLISH Document Type: MEETING ABSTRACT

7/3,AB/179 (Item 60 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci
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02972711 Genuine Article#: MR587 Number of References: 28 Title: HIGH-MOLECULAR-WEIGHT *HYALURONIC* ACIDS INHIBIT CHEMOTAXIS AND PHAGOCYTOSIS BUT NOT LYSOSOMAL-ENZYME RELEASE INDUCED BY RECEPTOR-MEDIATED STIMULATIONS IN GUINEA-PIG PHAGOCYTES (Abstract Available)

Author(s): TAMOTO K; NOCHI H; TADA M; SHIMADA S; MORI Y; KATAOKA S; SUZUKI Y; NAKAMURA T Corporate Source: HIGASHI NIPPON GAKUEN UNIV,FAC PHARMACEUT SCI,DEPT MICROBIOL,1757 AZA KANAZAWA/TOBETSU/HOKKAIDO06102/JAPAN/ Journal: MICROBIOLOGY AND IMMUNOLOGY, 1994, V38, N1, P73-80 ISSN: 0385-5600 Language: ENGLISH Document Type: ARTICLE Abstract: The effects of high-molecular-weight (HMW) hyaluronic acids (HAs) of 1.9x10(6) Da, 8x10(5) Da and 3x10(5) Da on the receptor-mediated functions of guinea pig peritoneal phagocytes were studied. HMW-HAs of 1.9x10(6) Da (HA190) and 8x10(5) Da (HA80) effectively inhibited the chemotactic activity of polymorphonuclear leukocytes (PMNs) for formyl-Met-Leu-Phe (fMLP). The degree of inhibition was dose-dependent and the concentrations of HA190 and HA80 required for 50% inhibition were 0.5-1.5 mg/ml and 1.5-2.5 mg/ml, respectively. HMW-HA of 3x10(5) Da (HA30) hardly affected the chemotaxis within a concentration range of 0.5-5.0 mg/ml. The phagocytic activities of PMNs and macrophages (M(phi)s) for serum-opsonized zymosan (SOZ) and polystyrene latex particles were also inhibited by these HAs in a dose- and molecular-weight-dependent manner and HA190 was again the most inhibitory. By contrast, the release of lysosomal enzyme from M(phi)s stimulated with SOZ was not significantly affected by HMW-HAs at any concentration used. Furthermore, the binding of [H-3]fMLP with PMNs and the rosette formation of M(phi)s with SOZ were not influenced by the presence of HMW-HAs. These findings suggested that the binding of HMW-HAs to the HA receptors on PMNs and M(phi)s might produce certain intracellular signals which would be responsible for the suppression of the chemotaxis and the phagocytosis but not for the release of lysosomal enzyme. For the generation of such signals,
higher-molecular-weight HMW-HAs would be more effective than lower one.

7/3,AB/180 (Item 61 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci

02964647 Genuine Article#: MU945 Number of References: 25 Title: ZONAL DISTRIBUTION OF *CHONDROITIN*-4-SULFATE DERMATAN SULFATE AND *CHONDROITIN*-6-SULFATE IN NORMAL AND DISEASED HUMAN SYNOVIUM (Abstract Available) Author(s): WORRALL JG; WILKINSON LS; BAYLISS MT; EDWARDS JCW Corporate Source: UCMSM,ARTHUR STANLEY HOUSE,TOTTENHAM ST/LONDON W1P 9PG//ENGLAND/; KENNEDY INST/LONDON W6 7DW//ENGLAND/ Journal: ANNALS OF THE RHEUMATIC DISEASES, 1994, V53, N1 (JAN), P35-38 ISSN: 0003-4967 Language: ENGLISH Document Type: ARTICLE Abstract: Objectives-Chondroitin sulphate is the major sulphated glycosaminoglycan present in the extracellular matrix of soft connective tissues and the aim of this study was to investigate the distribution of chondroitin sulphate species in normal and diseased synovium.

Methods-Distribution of chondroitin-4-sulphate/dermatan sulphate (Ch4S/DS) and chondroitin-6-sulphate in normal (n = 6), osteoarthritic (n = 4) and rheumatoid (n = 10) synovium was determined using an immunoperoxidase technique and specific monoclonal antibodies to chondroitinase ABC-digested preparations.

Results-Ch4S/DS was expressed throughout the interstitium of all tissues and was also present on blood vessels in rheumatoid samples only. Ch6S was expressed in the lining layer of normal synovium but was absent from this site in osteoarthritic and rheumatoid tissues. Ch6S was also present on all blood vessels in all tissues. Conclusions-The distinct zonal distributions of Ch4S/DS and Ch6S and their alteration in disease suggest these molecules have different and specific functions in normal and diseased synovium.

7/3,AB/181 (Item 62 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci

02884532 Genuine Article#: MM527 Number of References: 46 Title: *HYALURONAN* AND CD44 IN PSORIATIC SKIN - INTENSE STAINING FOR *HYALURONAN* ON DERMAL CAPILLARY LOOPS AND REDUCED EXPRESSION OF CD44 AND *HYALURONAN* IN KERATINOCYTE LEUKOCYTE INTERFACES (Abstract Available) Author(s): TAMMI R; PAUKKONEN K; WANG C; HORSMANHEIMO M; TAMMI M Corporate Source: UNIV KUOPIO,DEPT ANAT,BOX 1627/SF-70211 KUOPIO//FINLAND/; UNIV KUOPIO,DEPT DERMATOL/KUOPIO//FINLAND/ Journal: ARCHIVES OF DERMATOLOGICAL RESEARCH, 1994, V286, N1 (JAN), P21-29 ISSN: 0340-3696 Language: ENGLISH Document Type: ARTICLE Abstract: The distributions of hyaluronan (HA) and its presumptive receptor, CD44, were studied in skin samples from 13 psoriasis vulgaris patients, using an HA-specific probe (HABC), and monoclonal antibodies, respectively. The general distribution of HA and CD44 in psoriatic lesional epidermis resembled that in normal epidermis. However, areas of epidermis invaded by leukocytes showed a local depletion of HA and CD44,

particularly at the contact areas of keratinocytes to lymphocytes and neutrophils. Removal by cellular uptake or extracellular degradation of CD44 and HA may be required for tight adherence between a keratinocyte and a leukocyte. On the dermal side, the tips of the prolonged dermal papillae in psoriatic lesions were intensively stained with HABC. The dilated capillaries and the space below the tip basal lamina, in particular, were heavily covered with HA. Occasionally, a similar intense staining was seen around an enlarged capillary in uninvolved psoriatic skin. CD44-positive leukocytes were found around the affected capillaries. The accumulation of HA in the dermal papillae may support the growth of psoriatic lesions, since HA stimulates the growth of capillaries as well as attracting inflammatory cells.

7/3,AB/182 (Item 63 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci
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02382231 Genuine Article#: KX965 Number of References: 0 Title: A *HYALURONAN* *RECEPTOR* TERMED RHAMM CONTAINS *HYALURONAN* AND HEPARIN BINDING MOTIFS
Author(s): YANG BH; YANG BL; HALL C; SAVANI R; TURLEY EA
Corporate Source: UNIV MANITOBA,MANITOBA INST CELL BIOL/WINNIPEG R3E 0V9/MANITOBA/CANADA/; UNIV MANITOBA,DEPT PEDIAT/WINNIPEG R3E 0V9/MANITOBA/CANADA/
Journal: JOURNAL OF CELLULAR BIOCHEMISTRY, 1993, S17E (MAR 29), P166 ISSN: 0730-2312
Language: ENGLISH Document Type: MEETING ABSTRACT

7/3,AB/183 (Item 64 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci
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02382219 Genuine Article#: KX965 Number of References: 0 Title: MECHANISMS OF SMOOTH-MUSCLE CELL-MIGRATION - THE ROLE OF *HYALURONAN* (*HA*) AND THE *HA* *RECEPTOR* RHAMM Author(s): SAVANI RC; WANG C; YANG BH; KINSELLA M; WIGHT TN; STERN R; TURLEY EA
Corporate Source: DEPT PEDIAT/WINNIPEG R3E 0V9/MB/CANADA/; MANITOBA INST CELL BIOL/WINNIPEG R3E 0V9/MB/CANADA/
Journal: JOURNAL OF CELLULAR BIOCHEMISTRY, 1993, S17E (MAR 29), P163 ISSN: 0730-2312
Language: ENGLISH Document Type: MEETING ABSTRACT

7/3,AB/184 (Item 65 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci
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02382141 Genuine Article#: KX965 Number of References: 0 Title: EXPRESSION OF *HYALURONAN* (*HA*) AND THE *HA* *RECEPTOR* RHAMM FOLLOWING BLEOMYCIN-INDUCED LUNG INJURY
Author(s): SAVANI RC; WANG C; STERN R; KHALIL N; GREENBERG A; TURLEY E Corporate Source: MANITOBA INST CELL BIOL/WINNIPEG/MB/CANADA/ Journal: JOURNAL OF CELLULAR BIOCHEMISTRY, 1993, S17E (MAR 29), P138 ISSN: 0730-2312
Language: ENGLISH Document Type: MEETING ABSTRACT

7/3,AB/185 (Item 66 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci
(c) 2002 Inst for Sci Info. All rts. reserv.

02382085 Genuine Article#: KX965 Number of References: 0 Title: THE ROLE OF *HYALURONAN* *RECEPTOR* RHAMM IN CELL LOCOMOTION
Author(s): YANG B; KORNOVSKI BS; MOWAT M; TURLEY EA
Corporate Source: UNIV MANITOBA,MANITOBA INST CELL BIOL/WINNIPEG R3E 0V9/MANITOBA/CANADA/; UNIV MANITOBA,DEPT PEDIAT/WINNIPEG R3E 0V9/MANITOBA/CANADA/
Journal: JOURNAL OF CELLULAR BIOCHEMISTRY, 1993, S17E (MAR 29), P124 ISSN: 0730-2312
Language: ENGLISH Document Type: MEETING ABSTRACT

7/3,AB/186 (Item 67 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci
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02382035 Genuine Article#: KX965 Number of References: 0 Title: TGF-BETA REGULATION OF CELL LOCOMOTION IS MEDIATED BY THE *HYALURONAN* *RECEPTOR* RHAMM
Author(s): GREENBERG AH; SAMUEL SK; KHALIL N; SAVANI R; YANG BH; TURLEY EA Corporate Source: UNIV MANITOBA,MANITOBA INST CELL BIOL/WINNIPEG R3T 2N2/MANITOBA/CANADA/; UNIV MANITOBA,DEPT PEDIAT/WINNIPEG R3T 2N2/MANITOBA/CANADA/; UNIV MANITOBA,DEPT MED/WINNIPEG R3T 2N2/MANITOBA/CANADA/; UNIV MANITOBA,DEPT IMMUNOL/WINNIPEG R3T 2N2/MANITOBA/CANADA/
Journal: JOURNAL OF CELLULAR BIOCHEMISTRY, 1993, S17E (MAR 29), P110 ISSN: 0730-2312

Language: ENGLISH Document Type: MEETING ABSTRACT

7/3,AB/187 (Item 68 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci
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02357640 Genuine Article#: KW761 Number of References: 0 Title: *HYALURONAN* *RECEPTOR* EXPRESSION ON HUMAN PERIPHERAL-BLOOD MONOCYTES AND ALVEOLAR MACROPHAGES
Author(s): CULTY M; SWARTZ RP; UNDERHILL CB; YEAGER H
Corporate Source: GEORGE WASHINGTON UNIV,MED CTR/WASHINGTON//DC/20037 Journal: CLINICAL RESEARCH, 1993, V41, N2 (APR), PA315
ISSN: 0009-9279
Language: ENGLISH Document Type: MEETING ABSTRACT

7/3,AB/188 (Item 69 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci
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02356610 Genuine Article#: KW761 Number of References: 0 Title: DETECTION AND LOCALIZATION OF *HYALURONIC*-*ACID* *RECEPTOR* (CD44) EXPRESSION IN FINE-NEEDLE ASPIRATES FROM THYROID CANCERS (TC)
Author(s): HEUFELDER AE; BAHN RS
Corporate Source: UNIV MUNICH,KLINIKUM INNENSTADT,MED KLIN/W-8000MUNICH 2//GERMANY/; MAYO CLIN & MAYO FDN,DEPT INTERNAL MED,DIV ENDOCRINOL/ROCHESTER//MN/55905
Journal: CLINICAL RESEARCH, 1993, V41, N2 (APR), PA129
ISSN: 0009-9279
Language: ENGLISH Document Type: MEETING ABSTRACT

7/3,AB/189 (Item 70 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci
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01981915 Genuine Article#: JR255 Number of References: 0 Title: AGE-RELATED-CHANGES IN SERUM *HYALURONAN* (*HA*) LEVELS AND LIVER ENDOTHELIAL-CELL *HA* *RECEPTOR* ACTIVITY
Author(s): YANNARIELLOBROWN J; CHAPMAN SH; PAPPAS T; WEIGEL PH Corporate Source: UNIV TEXAS,MED BRANCH,DEPT HUMAN BIOL CHEM & GENET/GALVESTON//TX/77550
Journal: MOLECULAR BIOLOGY OF THE CELL, 1992, V3, S (SEP), PA326 ISSN: 1059-1524
Language: ENGLISH Document Type: MEETING ABSTRACT

7/3,AB/190 (Item 71 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci
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01980445 Genuine Article#: JR255 Number of References: 0 Title: IDENTIFICATION OF *HYALURONAN* BINDING MOTIFS IN A NOVEL *HYALURONAN* *RECEPTOR* TERMED RHAMM
Author(s): YANG B; ZHANG L; TURLEY EA
Corporate Source: UNIV MANITOBA,MANITOBA INST CELL BIOL/WINNIPEG R3E 0V9/MANITOBA/CANADA/; UNIV MANITOBA,DEPT PEDIAT/WINNIPEG R3E 0V9/MANITOBA/CANADA/
Journal: MOLECULAR BIOLOGY OF THE CELL, 1992, V3, S (SEP), PA73 ISSN: 1059-1524
Language: ENGLISH Document Type: MEETING ABSTRACT

7/3,AB/191 (Item 72 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci
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01622687 Genuine Article#: HM547 Number of References: 28 Title: THE ROLE OF *HYALURONAN*-BINDING PROTEIN IN ASSEMBLY OF PERICELLULAR MATRICES (Abstract Available)
Author(s): QIN Y; BANERJEE SD; TOOLE BP
Corporate Source: TUFTS UNIV,SCH HLTH SCI,DEPT ANAT & CELLULAR BIOL,HLTH SCI CAMPUS,136 HARRISON AVE/BOSTON//MA/02111; TUFTS UNIV,SCH HLTH SCI,DEPT ANAT & CELLULAR BIOL,HLTH SCI CAMPUS,136 HARRISON AVE/BOSTON//MA/02111
Journal: DEVELOPMENTAL DYNAMICS, 1992, V193, N2 (FEB), P145-151 Language: ENGLISH Document Type: ARTICLE
Abstract: Hyaluronan-dependent pericellular matrices or "coats" are expressed by a variety of cell types in culture and modulation of their expression may be important in regulation of cell interactions in vivo during development. Monoclonal antibody IVd4, which recognizes hyaluronan-binding protein with the properties of a *hyaluronan* *receptor*, was shown to block formation of these coats by a variety of cells. Using rat fibrosarcoma cells, it was found that the antibody not only blocked initial formation of the coats but also caused their loss when added subsequent to formation. The loss of preformed coats in the presence of antibody occurred at 4-degrees and 37-degrees,

implying that the function of hyaluronan-binding protein in coat formation is not in mediating metabolic processes. The antibody also had no significant effect on hyaluronan production by the fibrosarcoma cells. In addition, hyaluronan hexasaccharide, a competitive inhibitor of the interaction between polymeric hyaluronan and its cell surface receptor, was found to inhibit coat formation. Thus it is concluded that a hyaluronan-binding protein with the properties of a *hyaluronan* *receptor* is required for pericellular matrix formation.
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E9 37 YANNAS IOANNIS V/AU
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E11 3 YANNAS JOHN B/AU
E12 1 YANNASCOLI DONALD/AU

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=> s l1 and 1997/py

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L2 2 L1 AND 1997/PY

=> d ibib 1,2

L2 ANSWER 1 OF 2 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1998:93940 CAPLUS
DOCUMENT NUMBER: 128:226614
TITLE: Enhancement of corneal epithelial wound healing by thrombin receptor activating peptide in the rat AUTHOR(S): Hallberg, Csilla K.; Gill, Kuljit S.; Redin, William R.; *Yannariello-Brown, Judith* ; Brysk, Miriam M.; Carney, Darrell H.; Trocme, Stefan D. CORPORATE SOURCE: Department of Ophthalmology and Visual Sciences, School of Medicine, Cornea Service and Eye Research Laboratory, The University of Texas Medical Branch, Galveston, TX, 77555-0787, USA
SOURCE: Research Communications in Pharmacology and Toxicology (*1997*), 2(3), 129-136
CODEN: RCPTFY; ISSN: 1087-1101
PUBLISHER: PJD Publications Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

L2 ANSWER 2 OF 2 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1997:137101 CAPLUS
DOCUMENT NUMBER: 126:234877
TITLE: Identification of a 175 kDa protein as the ligand-binding subunit of the rat liver sinusoidal endothelial cell hyaluronan receptor AUTHOR(S): *Yannariello-Brown, Judith* ; Zhou, Bin; Weigel, Paul H.
CORPORATE SOURCE: Health Sciences Center, University of Oklahoma, Oklahoma City, OK, 73190, USA
SOURCE: Glycobiology (*1997*), 7(1), 15-21 CODEN: GLYCE3; ISSN: 0959-6658
PUBLISHER: Oxford University Press
DOCUMENT TYPE: Journal
LANGUAGE: English

CBA

=> d re.cnt 2

L2 ANSWER 2 OF 2 CAPLUS COPYRIGHT 2002 ACS

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E10 2 YANNELIS D/AU
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E12 13 YANNELLI B/AU

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L3 24 "YANNARIELLOBROWN J"/AU

=> s l3 and 1997/py
939176 1997/PY
L4 3 L3 AND 1997/PY

=> d ibib all

L4 ANSWER 1 OF 3 SCISEARCH COPYRIGHT 2002 ISI (R)
ACCESSION NUMBER: 97:232804 SCISEARCH
THE GENUINE ARTICLE: WN215
TITLE: Eosinophil cationic proteins modulate intercellular adhesion molecule-1 (ICAM-1; CD54) expression on primary human corneal epithelial cells.
AUTHOR: *YannarielloBrown J (Reprint)* ; Hallberg C K; Trocme S D
CORPORATE SOURCE: UNIV TEXAS, MED BRANCH, DEPT OPHTHALMOL, GALVESTON, TX 77550; UNIV TEXAS, MED BRANCH, DEPT HUMAN BIOL CHEM & GENET, GALVESTON, TX 77550
COUNTRY OF AUTHOR: USA
SOURCE: INVESTIGATIVE OPHTHALMOLOGY & VISUAL SCIENCE, (*15 MAR* * 1997*) Vol. 38, No. 4, Part 2, pp. 3352-3352. Publisher: LIPPINCOTT-RAVEN PUBL, 227 EAST WASHINGTON SQ, PHILADELPHIA, PA 19106.
ISSN: 0146-0404.
DOCUMENT TYPE: Conference; Journal
FILE SEGMENT: LIFE
LANGUAGE: English
REFERENCE COUNT: 0
AN 97:232804 SCISEARCH
GA The Genuine Article (R) Number: WN215
TI Eosinophil cationic proteins modulate intercellular adhesion molecule-1 (ICAM-1; CD54) expression on primary human corneal epithelial cells. AU *YannarielloBrown J (Reprint)* ; Hallberg C K; Trocme S D CS UNIV TEXAS, MED BRANCH, DEPT OPHTHALMOL, GALVESTON, TX 77550; UNIV TEXAS, MED BRANCH, DEPT HUMAN BIOL CHEM & GENET, GALVESTON, TX 77550 CYA USA
SO INVESTIGATIVE OPHTHALMOLOGY & VISUAL SCIENCE, (*15 MAR 1997*) Vol. 38, No. 4, Part 2, pp. 3352-3352.
Publisher: LIPPINCOTT-RAVEN PUBL, 227 EAST WASHINGTON SQ, PHILADELPHIA, PA 19106.
ISSN: 0146-0404.
DT Conference; Journal
FS LIFE
LA English
REC Reference Count: 0
CC OPHTHALMOLOGY

=> d all 2, 3

L4 ANSWER 2 OF 3 SCISEARCH COPYRIGHT 2002 ISI (R)
AN 97:154537 SCISEARCH
GA The Genuine Article (R) Number: WH475
TI Identification of a 175 kDa protein as the ligand-binding subunit of the rat liver sinusoidal endothelial cell hyaluronan receptor AU *YannarielloBrown J* ; Zhou B; Weigel P H (Reprint) CS UNIV OKLAHOMA, HLTH SCI CTR, DEPT BIOCHEM & MOL BIOL, OKLAHOMA CITY, OK 73190 (Reprint); UNIV OKLAHOMA, HLTH SCI CTR, DEPT BIOCHEM & MOL BIOL, OKLAHOMA CITY, OK 73190; UNIV TEXAS, MED BRANCH, DEPT OPHTHALMOL & VISUAL SCI, GALVESTON, TX 77555; UNIV TEXAS, MED BRANCH, DEPT HUMAN BIOL CHEM & GENET, GALVESTON, TX 77555 CYA USA

SO GLYCOBIOLOGY, (*FEB 1997*) Vol. 7, No. 1, pp. 15-21. Publisher: OXFORD UNIV PRESS UNITED KINGDOM, WALTON ST JOURNALS DEPT, OXFORD, ENGLAND OX2 6DP.
ISSN: 0959-6658.
DT Article; Journal
FS LIFE
LA English
REC Reference Count: 26
AB The rat liver sinusoidal endothelial cell (LEG) hyaluronan (HA) receptor was previously identified using a photoaffinity HA derivative (J. Biol, Chem., 267, 20451-20456, 1992), Two polypeptides with M(r) = 175,000 and 166,000, were consistently crosslinked, suggesting that the LEC HA receptor is an oligomer, Whether one or both subunits participate in HA binding, was not determined, Here we investigate the HA-subunit interactions and the potential oligomeric nature of the LEC HA receptor, When Sephacryl-400 gel filtration chromatography was used to enrich the HA receptor, the 175 kDa polypeptide was the major band seen by SDS-PAGE analysis, Little staining was seen at 166 kDa, suggesting that the 175 kDa protein could be separated from the 166 kDa protein and still retain HA-binding activity, A ligand blot assay was used to determine if each individual subunit could bind HA, LEC proteins were separated by nonreducing SDS-PAGE, and then immobilized onto nitrocellulose. I-125-HA bound to a 175 kDa polypeptide but not to the 166 kDa protein, A high molecular weight band of similar to 300,000 also bound I-125-HA. I-125-HA binding to the 175 and 300 kDa proteins showed the same specificity of competition with a panel of carbohydrates as the bona fide LEC HA receptor, The 175 kDa HA-binding subunit may be nonglobular (asymmetric), since its apparent size by SDS-PAGE is dependent on the polyacrylamide gel pore size; M(r) increases as porosity decreases, LECs were crosslinked to an I-125-labeled photoaffinity HA derivative and the HA saccharides were then released with hyaluronidase. After SDS-PAGE without reduction, radio-labeled bands were seen at 175 and 166 kDa (3:1 ratio), and a high MW (similar to 300,000) species was also detected, These data support an oligomeric model of the LEC HA receptor, and show that the 175 kDa protein possesses HA-binding activity independent from the 166 kDa polypeptide. CC BIOCHEMISTRY & MOLECULAR BIOLOGY
ST Author Keywords: hyaluronan receptor; endocytosis; ligand blot assay; liver sinusoidal endothelial cells
STP KeyWords Plus (R): ACID; DEGRADATION; DISTINCT; SURFACE RF 95-1163 001; CD44 ISOFORMS; DIFFERENTIAL EXPRESSION; INDEPENDENT PROGNOSTIC FACTOR
95-2761 001; CHONDROITIN SULFATE PROTEOGLYCANS; BASIC FIBROBLAST GROWTH-FACTOR; HIGH-PERFORMANCE CAPILLARY ELECTROPHORESIS 95-3190 001; INCREASED ABUNDANCE OF SPECIFIC SKELETAL-MUSCLE PROTEIN-TYROSINE PHOSPHATASES; ALPHA-B-CRYSTALLIN EXPRESSION 95-5491 001; SERUM HYALURONAN; SINUSOIDAL LIVER ENDOTHELIAL-CELLS; DETECTION OF HEPATIC FIBROGENESIS; KIDNEY ULTRAFILTRATION; CIRCULATING COLLAGEN
RE

Referenced Author	Year	VOL	PG	Referenced Work (RAU)	(RPY)	(RVL)	(RPG)	(RWK)
BITTER T	1962	4	330	ANAL BIOCHEM				
BRADFORD M M	1976	72	248	ANAL BIOCHEM				
DSOUZA M	1985	10	43	BIOCHEM INT				
ERIKSSON S	1983	144	223	EXP CELL RES				
FORSBERG N	1991	1078	12	BIOCHIM BIOPHYS ACTA FROST S J	1992	189	1591	BIOCHEM BIOPH RES CO KNUDSON C B
	1993	120	825	J CELL BIOL				
LAEMMLI U K	1970	277	680	NATURE				
LAURENT T C	1987	143		CIBA S F				
LAURENT T C	1992	6	2397	FASEB J				
LOWRY O H	1981	193	265	J BIOL CHEM				
MCCOURT P A G	1994	269	30081	J BIOL CHEM				
MCGARY C T	1989	257	875	BIOCHEM J				
OKA J A	1987	133	243	J CELL PHYSIOL				
RAJA R H	1984	139	168	ANAL BIOCHEM				
RAJA R H	1988	263	16661	J BIOL CHEM				
SMEDSROD B	1984	223	617	BIOCHEM J				
SMEDSROD B	1990	266	313	BIOCHEM J				
STAD R K	1994	2	261	CELL ADHES COMMUN TOOLE B P	1990	2	839	CURR OPIN CELL BIOL
UNDERHILL C	1992	103	293	J CELL SCI				
WEIGEL P H	1992		421	GLYCOCONJUGATES COMP YANNARIELLOBROW.J	1996	218	314	BIOCHEM BIOPH RES CO YANNARIELLOBROWN J
	1992	31	576	BIOCHEMISTRY-US YANNARIELLOBROWN J				

|1992 |267 |20451 |J BIOL CHEM
YANNARIELLOBROWN J |1992 |48 |73 |J CELL BIOCHEM

L4 ANSWER 3 OF 3 SCISEARCH COPYRIGHT 2002 ISI (R)
AN 97:35597 SCISEARCH
GA The Genuine Article (R) Number: WA059
TI ICAM-1 expression in corneal epithelium of a patient with vernal keratoconjunctivitis: Case report
AU Gill K S; *YannarielloBrown J* ; Patel J; Nakajima N; Rajaraman S; Trocme S D (Reprint)
CS UNIV TEXAS, MED BRANCH, DEPT OPHTHALMOL & VISUAL SCI, SCH MED, CLIN SCI BLDG, ROOM 340, GALVESTON, TX 77555 (Reprint); UNIV TEXAS, MED BRANCH, DEPT OPHTHALMOL & VISUAL SCI, SCH MED, GALVESTON, TX 77555 CYA USA
SO CORNEA, (*JAN 1997*) Vol. 16, No. 1, pp. 107-111. Publisher: LIPPINCOTT-RAVEN PUBL, 227 EAST WASHINGTON SQ, PHILADELPHIA, PA 19106.
ISSN: 0277-3740.
DT Article; Journal
FS CLIN
LA English
REC Reference Count: 24
AB Recent reports have demonstrated the expression of intercellular adhesion molecule-1 (ICAM-1; CD54) on the epithelium in various allergic diseases and inflammatory conditions, including the bronchial epithelium of patients with allergic asthma, conjunctival epithelium of allergic patients after allergen-specific challenge, and corneal epithelium of rejected corneal allografts. We investigated the presence of ICAM-1 expression on the corneal epithelium from a patient with vernal keratoconjunctivitis (VKC). Immunohistochemical staining of the diseased cornea demonstrated abundant ICAM-1 expression on the corneal epithelium. Immunoreactive ICAM-1 appeared to localize primarily to the cells of the basal and middle layers of the corneal epithelium. No staining was detected on the ocular surface epithelium. The normal, healthy cornea demonstrated no significant ICAM-1 expression on any of the epithelial layers, similar to that previously reported. To the best of our knowledge, this is the first report of ICAM-1 expression on the corneal epithelium from a patient with VKC.
CC OPHTHALMOLOGY
ST Author Keywords: allergy; CD54; corneal epithelium; inflammation; intercellular adhesion molecule-1; vernal keratoconjunctivitis STP KeyWords Plus (R): MAJOR BASIC-PROTEIN; INTERCELLULAR-ADHESION MOLECULE; MONOCLONAL-ANTIBODIES; CD54; INFLAMMATION; CONJUNCTIVA; DEPOSITION; CHALLENGE; LFA-1; CELLS
RF 95-0169 001; INTERCELLULAR-ADHESION MOLECULE-1 (ICAM-1); ENDOTHELIAL-CELL REGULATION OF LEUKOCYTE INFILTRATION; ONCOSTATIN-M ENHANCE MEMBRANE EXPRESSION
RE

Referenced Author	Year	VOL	PG	Referenced Work (RAU)	(RPY)	(RVL)	(RPG)	(RWK)
ALBELDA S M	1994	8	504	FASEB J				
BLOEMEN P G	1993	9	586	AM J RESP CELL MOL B BUCKLEY R J	1988	28	303	INT
OPHTHALMOL CLIN CANONICA G W	1994	49	135	ALLERGY				
CIPRANDI G	1993	91	783	J ALLERGY CLIN IMMUN CIPRANDI G	1995	95	612	J ALLERGY CLIN
IMMUN ELIAS J M	1989	92	62	AM J CLIN PATHOL ELNER V M	1991	138	525	AM J PATHOL
FOETS B J J	1992	76	205	BRIT J OPHTHALMOL GOLDBERG M F	1994	101	161	OPHTHALMOLOGY
GOSSET P	1995	106	69	INT ARCH ALLERGY IMM HARLAN J M	1992		117	ADHESION ITS
ROLE IN HOBDEN J A	1995	36	1107	INVEST OPHTH VIS SCI LEFF A R	1991	260	L189	AM J
PHYSIOL								
PHILIPP W	1994	232	87	GRAEF ARCH CLIN EXP ROTHLEIN R	1986	137	1270	J IMMUNOL
SMOLIN G	1986		135	OCULAR IMMUNOLOGY SPRINGER T A	1990	346	425	NATURE
TROCME S D	1989	108	57	AM J OPHTHALMOL TROCME S D	1993	115	640	AM J OPHTHALMOL
TROCME S D	1992	67	557	MAYO CLIN PROC				
UDELL I J	1981	92	824	AM J OPHTHALMOL VORKAUF M	1993	231	323	GRAEF ARCH CLIN
EXP WHITCUP S M	1995	60	597	EXP EYE RES				

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=> d bib hit 1-9

L5 ANSWER 1 OF 9 CAPLUS COPYRIGHT 2002 ACS
AN 2002:465415 CAPLUS
TI The hyaluronan receptor for endocytosis (HARE) is not CD44 or CD54 (ICAM-1)
AU Weigel, Janet A.; Raymond, Robert C.; Weigel, Paul H. CS The Oklahoma Center for Medical Glycobiology, Department of Biochemistry and Molecular Biology, University of Oklahoma Health Sciences Center, Oklahoma City, OK, 73190, USA
SO Biochemical and Biophysical Research Communications (2002), 294(4), 918-922
CODEN: BBRCA9; ISSN: 0006-291X
PB Elsevier Science
DT Journal
LA English
RE.CNT 33 THERE ARE 33 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT
(29) Yannariello-Brown, J; Glycobiology 1997, V7, P15 CAPLUS
L5 ANSWER 2 OF 9 CAPLUS COPYRIGHT 2002 ACS
AN 2000:886047 CAPLUS
DN 135:40847
TI Improvement of Schwann cell attachment and proliferation on modified hyaluronic acid strands by polylysine
AU Hu, Min; Sabelman, Eric E.; Tsai, Charlotte; Tan, Jasmine; Hentz, Vincent R.
CS Functional Restoration Department, Medical School, Stanford University, Stanford, CA, USA
SO Tissue Engineering (2000), 6(6), 585-593
CODEN: TIENFP; ISSN: 1076-3279
PB Mary Ann Liebert, Inc.
DT Journal
LA English
RE.CNT 29 THERE ARE 29 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT
(29) Yannariello, B; Glycobiology 1997, V7, P15
L5 ANSWER 3 OF 9 CAPLUS COPYRIGHT 2002 ACS
AN 2000:871362 CAPLUS
DN 134:83882
TI Identification of the hyaluronan receptor for endocytosis (HARE) AU Zhou, Bin; Weigel, Janet A.; Fauss, LeAnn; Weigel, Paul H. CS Department of Biochemistry & Molecular Biology, University of Oklahoma Health Sciences Center, Oklahoma City, OK, 73190, USA SO Journal of Biological Chemistry (2000), 275(48), 37733-37741 CODEN: JBCHA3; ISSN: 0021-9258
PB American Society for Biochemistry and Molecular Biology DT Journal
LA English
RE.CNT 63 THERE ARE 63 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT
(60) Yannariello-Brown, J; Glycobiology 1997, V7, P15 CAPLUS
L5 ANSWER 4 OF 9 CAPLUS COPYRIGHT 2002 ACS
AN 2000:763025 CAPLUS
DN 134:27741
TI Hyaluronan. Is bigger better?
AU Camenisch, Todd D.; McDonald, John A.

CS Departments of Biochemistry and Molecular Biology, Mayo Clinic Scottsdale, Scottsdale, AZ, 85259, USA
SO American Journal of Respiratory Cell and Molecular Biology (2000), 23(4), 431-433
CODEN: AJRBEL; ISSN: 1044-1549
PB American Thoracic Society
DT Journal; General Review
LA English
RE.CNT 42 THERE ARE 42 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT
(40) Yannariello-Brown, J; Glycobiology 1997, V7, P15 CAPLUS
L5 ANSWER 5 OF 9 CAPLUS COPYRIGHT 2002 ACS
AN 1999:812416 CAPLUS
DN 132:120271
TI How does the hyaluronan scrap-yard operate?
AU McCourt, Peter A. G.
CS Department of Experimental Pathology, Institute for Medical Biology, University of Tromso, Tromso, N-9037, Norway
SO Matrix Biology (1999), 18(5), 427-432
CODEN: MTBOEC; ISSN: 0945-053X
PB Elsevier Science B.V.
DT Journal; General Review
LA English
RE.CNT 52 THERE ARE 52 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT
(50) Yannariello-Brown, J; Glycobiology 1997, V7, P15 CAPLUS
L5 ANSWER 6 OF 9 CAPLUS COPYRIGHT 2002 ACS
AN 1999:777661 CAPLUS
DN 132:89737
TI Purification and subunit characterization of the rat liver endocytic hyaluronan receptor
AU Zhou, Bin; Oka, Janet A.; Singh, Anil; Weigel, Paul H. CS Department of Biochemistry and Molecular Biology, University of Oklahoma Health Sciences Center, Oklahoma City, OK, 73190, USA SO Journal of Biological Chemistry (1999), 274(48), 33831-33834 CODEN: JBCHA3; ISSN: 0021-9258
PB American Society for Biochemistry and Molecular Biology DT Journal
LA English
RE.CNT 31 THERE ARE 31 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT
(28) Yannariello-Brown, J; Glycobiology 1997, V7, P15 CAPLUS
L5 ANSWER 7 OF 9 CAPLUS COPYRIGHT 2002 ACS
AN 1999:750638 CAPLUS
DN 132:149451
TI Characterization of a hyaluronan receptor on rat sinusoidal liver endothelial cells and its functional relationship to scavenger receptors AU McCourt, Peter A. G.; Smedsrod, Bard H.; Melkko, Jukka; Johansson, Staffan CS Department of Experimental Pathology, University of Tromso, Tromso, N-9037, Norway
SO Hepatology (Philadelphia) (1999), 30(5), 1276-1286
CODEN: HPTLD9; ISSN: 0270-9139
PB W. B. Saunders Co.
DT Journal
LA English
RE.CNT 58 THERE ARE 58 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT
(57) Yannariello-Brown, J; Glycobiology 1997, V7, P15 CAPLUS
L5 ANSWER 8 OF 9 CAPLUS COPYRIGHT 2002 ACS
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DN 132:34482
TI Mapping the interaction between murine IgA and murine secretory component carrying epitope substitutions reveals a role of domains II and III in covalent binding to IgA
AU Crottet, Pascal; Corthesy, Blaise
CS Institut Suisse de Recherches Experimentales sur le Cancer, Epalinges, CH-1066, Switz.

SO Journal of Biological Chemistry (1999), 274(44), 31456-31462 CODEN: JBCHA3; ISSN: 0021-9258
PB American Society for Biochemistry and Molecular Biology DT Journal
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RE.CNT 36 THERE ARE 36 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT
(35) Yannariello-Brown, J; Glycobiology 1997, V7, P15 CAPLUS
L5 ANSWER 9 OF 9 CAPLUS COPYRIGHT 2002 ACS
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TI Polypeptide resurfacing method improves fibroblast's adhesion to hyaluronan strands
AU Hu, Min; Sabelman, Eric E.; Lai, Susan; Timek, Ewa K.; Zhang, Feng; Hentz, Vincent R.; Lineaweaver, William C.
CS Department of Functional Restoration, Stanford University, Palo Alto, CA, 94305, USA
SO Journal of Biomedical Materials Research (1999), 47(1), 79-84 CODEN: JBMRBG; ISSN: 0021-9304
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L6 4 YANNARIELLO

=> d fp, ren, rep 1-4

L6 ANSWER 1 OF 4 USPATFULL
United States Patent Patent Number: 5902795 Date of Patent: 11 May 1999

Oligosaccharides reactive with hyaluronan-binding protein and their methods of use

Inventor(s): Toole, Bryan P., Watertown, MA, United States Banerjee, Shib D., Melrose, MA, United States
Assignee: Trustees of Tufts College, Medford, MA, United States (U.S. corporation)
Appl. No.: 94-306150
Filed: 14 Sep 1994

Publication Details

PATENT INFORMATION: US 5902795 11 May 1999

Related U.S. Application Data

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Issue U.S. Cl. ..... 514/054.000; 514/002.000; 514/004.000; 514/061.000 Current U.S. Cl. ..... 514/054.000; 514/002.000; 514/004.000; 514/061.000 Field of Search 514/54; 514/61; 514/2; 514/4

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Primary Examiner - Fonda, Kathleen K.
Attorney, Agent or Firm - Hamilton, Brook, Smith & Reynolds, P.C.

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41 Claim(s), 26 Drawing Figure(s), 10 Drawing Page(s)

ABSTRACT

Hyaluronan-binding protein (HABP) is expressed on the cell surface during tumor cell and endothelial cell migration and during capillary-like tubule formation. Monoclonal antibodies and hyaluronan oligosaccharides are described which specifically recognize HABP and can be used to (1) inhibit tumor growth by preventing tumor vascularization, (2) inhibit tumor cell migration and (3) image tumors.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

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REP WO 9420115 Sep 1994

L6 ANSWER 2 OF 4 USPATFULL

United States Patent Patent Number: 5703205 Date of Patent: 30 Dec 1997

Laminin a chain polypeptides from the amino terminal golbular domain

Inventor(s): Skubitz, Amy P. N., Minneapolis, MN, United States Furcht, Leo T., Minneapolis, MN, United States
Assignee: Regents of the University of Minnesota, Minneapolis, MN, United States (U.S. corporation)

Appl. No.: 93-72283
Filed: 7 Jun 1993

Publication Details

PATENT INFORMATION: US 5703205 30 Dec 1997

Related U.S. Application Data

Continuation of Ser. No. US 1992-895252, filed on 8 Jun 1992, now patented, Pat. No. US 5276136, Pat. No. 5276136 which is a continuation of Ser. No. US 1991-646291, filed on 25 Jan 1991, now abandoned

Int. Cl. ..... A61K038-00; C07K007-00; C07K007-10; C07K007-06 Issue U.S. Cl. 530/324.000; 530/326.000; 530/327.000; 530/330.000; 514/012.000; 514/013.000
Current U.S. Cl. ..... 530/324.000; 530/326.000; 530/327.000; 530/330.000 Field of Search 530/326; 530/324; 530/327; 514/14; 514/13; 514/12

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US 4870160	Sep 1989	530/326.000	Charonis et al.
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Art Unit - 181
Primary Examiner - Tsang, Cecilia J.
Assistant Examiner - Marshall, S.
Attorney, Agent or Firm - Merchant, Gould, Smith, Edell, Welter & Schmidt

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1 Claim(s), 11 Drawing Figure(s), 11 Drawing Page(s)

ABSTRACT

Polypeptides derived from domain VI of the amino terminal globule of the A chain of laminin and having sequences of at least about 5 amino acids, and which exhibit cell adhesion and cell spreading capacity are described.

Medical devices such as prosthetic implants, per-cutaneous devices and cell culture substrates coated with a composition including the described polypeptides are also provided.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

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EP 244688 Nov 1987

L6 ANSWER 3 OF 4 USPATFULL

United States Patent Patent Number: 5276136 Date of Patent: 4 Jan 1994

Laminin A chain polypeptides from the amino terminal globular domain

Inventor(s): Skubitz, Amy P. N., Minneapolis, MN, United States Furcht, Leo T., Minneapolis, MN, United States

Assignee: Regents of the University of Minnesota, Minneapolis, MN, United States (U.S. corporation)

Appl. No.: 92-895252

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Issue U.S. Cl. 530/326.000; 530/327.000

Current U.S. Cl. 530/326.000; 530/327.000

Field of Search 530/326; 530/327; 514/14; 514/13

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Art Unit - 181
Primary Examiner - Cashion, Jr., Merrell C.
Assistant Examiner - Marshall, S. G.
Attorney, Agent or Firm - Merchant, Gould, Smith, Edell, Welter & Schmidt

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5 Claim(s), 11 Drawing Figure(s), 11 Drawing Page(s)

ABSTRACT

Polypeptides derived from domain VI of the amino terminal globule of the A chain of laminin and having sequences of at least about 5 amino acids, and which exhibit cell adhesion and cell spreading capacity are described.

Medical devices such as prosthetic implants, percutaneous devices and cell culture substrates coated w

GOVERNMENT SUPPORT

This invention was made with government support under contract No. CA-29995 by the U.S. National Institutes of Health. The government has certain rights in the invention.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

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L6 ANSWER 4 OF 4 USPATFULL
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Laminin a chain polypeptides from the carboxy terminal globular domain
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ABSTRACT

Polypeptides derived from the G domain of the A chain of laminin and having sequences of at least about 5 amino acids, and which exhibit heparin/glycosaminoglycan binding, cell adhesion and cell spreading capacity are described.

Medical devices such as prosthetic implants, percutaneous devices and cell culture substrates coated with a composition including the described polypeptides are also provided.

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